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CONTRIBUTORS TO VOLUME VI

(*Key to initials given at end of each review and abstract*)

A. E. B. H.	A. E. B. Harding, B.A.
A. E. Q.	A. E. Quine, F.R.C.S.
A. J. W.	A. J. Walton, M.S., F.R.C.S., M.B., L.R.C.P., B.Sc.
B. D. W.	B. D. Watters, B.Sc.
C. C. C.	C. C. Choyce, C.M.G., C.B.E., F.R.C.S.
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C. F. M.	C. F. Marshall, F.R.C.S.
C. G. L. W.	C. G. L. Wolf, M.D.
C. L.	C. Lillingston, M.D.
C. L. E.	C. Lovatt Evans, D.Sc., M.R.C.S., L.R.C.P.
E. K. M.	E. K. Martin, M.S., F.R.C.S.
E. M. W.	Eva Muriel White, M.R.C.S., L.R.C.P., D.M.R.E.
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F. E. R.	F. E. Rockman.
F. J. F. B.	F. J. F. Barrington, F.R.C.S.
F. M. R. W.	F. M. R. Walshe, M.D., F.R.C.P.
G. E. O. W.	Gwynne E. O. Williams, M.S.
G. T. W.	G. T. Western, M.D.
G. W.	Gordon Ward, M.D.
H. D.	Haldin Davis, F.R.C.S., M.R.C.P.
H. W. D.	H. W. Dudley, O.B.E., M.Sc., Ph.D.
J. B. H.	J. B. Hunter, M.C., M.Ch., F.R.C.S.
J. D. R.	J. D. Rolleston, M.D.
J. H. B.	J. H. Burn, M.A., M.B.
J. H. D. W.	J. H. Douglas Webster, M.D., M.R.C.P.E.
J. P.	J. Parkinson, M.D.
J. R. P.	J. R. Perdrau, M.B., B.S., M.R.C.S., L.R.C.P.
J. T.	Julian Taylor, O.B.E., M.S., F.R.C.S.
M. B. D.	Maud B. Davis.
O. L. V. de W.	O. L. V. de Wesselow, M.B., B.Ch., M.R.C.P.
P. F.	P. Fildes, O.B.E., M.B., B.C.
P. L.-B.	P. Lazarus-Barlow, M.B., B.Ch.
R. A. P.	R. A. Peters, M.C., M.B., B.C.
S. E. L.-B.	Sarah E. Lazarus-Barlow.
S. R.	Sidney Russ, D.Sc.
S. U. L.-B.	Sybil U. Lazarus-Barlow.
T. W. P. L.	T. W. P. Lawrence, F.R.C.S.
W. A. M. S.	W. A. M. Smart, M.R.C.S., L.R.C.P., B.Sc.
W. B.	W. Bulloch, M.D., LL.D., F.R.S.
W. C.	W. Cramer, Ph.D., D.Sc., M.R.C.S., L.R.C.P.
W. S. L.-B.	W. S. Lazarus-Barlow, M.D., F.R.C.P.
W. W. C. T.	W. W. C. Topley, M.D., F.R.C.P.

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All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

WHOOPING-COUGH

Epidemiology. According to Henry, epidemiologist to the Massachusetts Department of Public Health, from 1913 to 1919 inclusive there were in Massachusetts 2,091 deaths from measles among 152,877 reported cases, while during the same period there were 2,384 deaths among 37,637 cases of whooping-cough, yielding a mortality rate of 1·3 per cent. for measles and over 6 per cent. for whooping-cough. From 1913 to 1918 90 per cent. of the deaths from whooping-cough and 79½ per cent. of those from measles were in children under 3 years of age. The mortality rates for the group under 3 in 1918 were 23½ per cent. for whooping-cough and 8 per cent. for measles. For each 1,000 cases of measles reported in Massachusetts during 1918 there were 18 deaths, and 14 of these were under In the same year there were 92 deaths among each 1,000 cases of whooping-cough, and 77 of the 92 were under 3. Even though there was, on an average, four or five times as much measles, the whooping-cough fatality rate for the period 1913–18 led the way with 2,065 deaths as compared with 1,908 deaths in the case of measles. There was thus a total of 3,973 deaths from the two diseases, 3,378 of which were under 3. Measles was more prevalent but less fatal, and whooping-cough less prevalent but more fatal. In the end the two diseases each caused an almost equal number of deaths.

Auchier, in his Paris thesis, has collected from various Paris hospitals statistics of whooping-cough mortality ranging from 37 per cent. at the Hôpital des Enfants Malades in 1867 to 4·36 per cent. at the Enfants Assistés in 1890–1900.

Symptomatology. Phillips, of Cleveland, Ohio, reports two cases of *whooping-cough contracted at the time of birth*, the infant in each case being infected by the obstetric nurse who was in the first week of her attack of pertussis, the nature of which was not recognized. He adds that it should be a golden rule that a nurse who has a cough should not attend an obstetric case, and states that in the course of a year, in three different families, he saw six cases of pertussis contracted from nurses who had coughs supposed to be due to ordinary colds. According to Phillips, whooping-cough during the first month of life may be congenital, as in the cases reported by Sir Thomas Watson and Rilliet and Barthez, but the majority of cases are acquired, especially as the incubation period may be very short.

The occurrence of *whooping-cough in the adult* forms the subject of papers by Hennes, Schwenkenbecher, and Neurath. According to Hennes,

whose four children were infected by an adult in whom the disease was not recognized, adults suffering from pertussis have a much larger share in the dissemination of the disease than has hitherto been supposed. He maintains that the virus undergoes an alteration in the adult in whom it becomes non-infectious for other adults, and it is only after passage through children that it becomes contagious for adults again. This theory, however, of the attenuated infectivity of whooping-cough in the adult, is not confirmed by the experience of Schwenkenbecher, who relates how in 1912 he developed pertussis after he had been attending the large whooping-cough department of the Frankfort hospital for nearly two years, and shortly afterwards infected his two children, aged 3 years and 12 months respectively. Nine years later his mother, who was suffering from an obstinate cough, infected all the other members of his family who had escaped in 1912. The mother and father, aged 80, had been infected by another son, aged 40, who had contracted the disease from a clerk in the same office, aged 23. Neurath, whose child had been infected by its nurse at the age of 5 months, maintains that pertussis in adults is a distinctly milder disease than in children, and indeed that the whole picture is usually transformed out of all recognition. There are only short convulsive explosions without a staccato character, like a laryngeal cough but without hoarseness. In neurotic individuals, on the other hand, the paroxysms retain the characteristic features which tend to be absent in normal persons with a robust nervous system.

In his work on the clinical aspects and epidemiology of pertussis, which is based on the study of about 25,000 cases in the course of nineteen years at the Francis Joseph Childrens' Hospital at Vienna, Pospischill states that *bronchiectasis* in some epidemics was an almost constant finding *post mortem*, though a number of years might pass without a single case being seen. He never met with a single case of pertussis in which the classical symptoms of bronchiectasis in the adult developed, the process always subsiding as recovery took place.

The epidemics in which bronchiectasis was found were also remarkable for the frequency of *clubbed fingers and toes*, which differed from those met with in congenital heart disease, empyema, and phthisis, in which the part of the terminal phalanx covered by the nail is most affected, by the thickening of the phalanx being most marked behind the nail.

Hauser records two cases showing that as the result of severe whooping-cough *cardiac changes* may occur, principally in the left ventricle but also in the right ventricle, in the form of well-marked dilatation and hypertrophy, which later may lead to alarming attacks of transient cardiac failure and even acute cardiac death. He recommends that the possibility of these cardiac changes should be borne in mind in every case of severe pertussis, especially when there is an otherwise inexplicable anaemia or general weakness and dyspnoea on exertion.

Pospischill found that *pyaemia* was a frequent occurrence in pertussis, though it was often not discovered until the autopsy. Most of the cases occurred in quite young children with severe pulmonary and cerebral involvement, often but not necessarily followed by accidental infections, especially ecthyma gangraenosum. In some cases the pyaemia was manifested by numerous abscesses in the internal organs, especially the lungs and kidneys, or a single organ might be affected by one or more abscesses. Empyema, purulent pericarditis, and purulent peritonitis were examples of

the isolated location of pertussis pyaemia. Articular metastases were usually found in a single joint only without any other pyaemic manifestations. The large joints were almost always implicated, especially those of the knee and hip. The most interesting pyaemic manifestation observed by Pospischill was fracture of the ribs with suppuration at the site of the fracture, of which he saw about a dozen examples, all ending fatally. He attributes this localization to the frequent handling of the rickety children, and especially friction during and after the numerous baths which formed an essential part of the treatment.

Among the accidental infections of pertussis Pospischill describes under the name of *aphthoid* a vesicular eruption which affects the buccal mucosa, tongue, larynx, and skin of the face, where it shows a predilection for the nostrils and lips. In some cases the lesions heal very rapidly, while others take a very protracted course and give rise to deep ulceration, or present the appearance of cancrum oris. In many cases symptoms of laryngeal obstruction arise necessitating tracheotomy.

Whooping-cough and tuberculosis. Pospischill states that among the many thousand autopsies which he has performed he has never found anything to indicate that tuberculosis had been aggravated by pertussis, but has rather been struck by the rarity of tuberculous lesions generally in cases of pertussis, and especially by the extremely small number of examples of active disease. Cases in which tuberculosis was shown by the autopsy to be the cause of death were extremely exceptional, especially after exclusion of concurrent measles, and it was only within the last two years that, as a result of the war, there had been an increase of tuberculosis. He therefore comes to the conclusion that no specific relation exists between whooping-cough and tuberculosis, and that if the doctor makes it a principle never to diagnose tuberculosis in a whooping-cough patient he is most likely to be correct.

Diagnosis. Meyer, of Copenhagen, states that, since the opening, in February 1916, of the whooping-cough diagnosis department of the State Serum Institute, 1,665 tests have been carried out with the following method. The suspected patient is made to cough towards, but not expectorate into, an aluminium box containing a medium composed of potato blood agar. The box is then placed in the incubator and in positive cases colonies of pertussis bacilli will be found in two or three days. The organisms are most likely to be present in the early stage of the disease, while the longer the whooping-cough lasts the less likely they are to be found, as is shown by the following figures: of 134 patients in the catarrhal stage 100, or 75 per cent., showed pertussis bacilli; of 673 in the first three weeks of the paroxysmal stage 365, or 54 per cent., gave a positive result; and of 107 who had the cough for more than five weeks only 10, or 9 per cent., were positive.

Modigliani and de Villa, of the Paediatric Clinic of the University of Rome, have employed an intradermo-reaction by means of an autolysat of a culture of the Bordet-Gengou bacillus with the following results: (1) The reaction was negative in 50 children suffering from various diseases but free from pertussis. (2) 38 children aged from 5 months to 6 years with active pertussis all gave a positive reaction, but no reaction was obtained with an autolysat of *B. coli* used as a control. (3) 10 children who had recovered from pertussis or in whom the disease had lasted over two months gave a negative or very feeble reaction. (4) The reaction

was intensely positive in three children who had been exposed to infection a few days before they developed definite symptoms of the disease.

Treatment. To prevent the spread of other diseases which are in the incubation stage on admission to hospital Pospischill isolates all new arrivals in small wards, as there are no single-bedded rooms available, for a period of 18 days, and on the 19th day admits them to large wards where they remain until their discharge.

His treatment consists in keeping the patients in the open air day and night in all seasons except in stormy or foggy weather, and the frequent use of hot baths followed by cold affusions together with hypodermic injections of morphia in restless cases. No age or concurrent disease, such as scarlet fever and measles in the eruptive stage, or laryngeal diphtheria, and even recent cases of intubation or tracheotomy, is regarded as a contra-indication to open-air treatment. Pospischill has abandoned the use of lumbar puncture, of which he made an extensive use at first, both for diagnostic and therapeutical purposes, as it did not appear to have any favourable influence, or indeed any effect at all, upon the convulsions of whooping-cough, for which it has been recommended by some authorities.

The treatment of whooping-cough by intramuscular injection of ether as recommended by French writers (vide *Medical Science*, 1921, **4**, 202–3) finds adherents in Spain in Vargas and Laramendi, and in Italy in d'Aroma, as well as in Tartrou in France. The last writer maintains that the method is efficacious only in cases of pure whooping-cough, and cannot be expected to be successful in those complicated by adenoids.

Veronese, of the Padua Paediatric Clinic, who employed the method in 10 cases, while admitting that the injections help to diminish the gravity of the disease, has come to the conclusion that the method does not constitute a great advance in the treatment of pertussis.

Auricchio, of the Naples University Institute of Clinical Paediatrics, also reports unfavourably of the method from his experience of it in 24 cases, all but three of which derived no benefit from the treatment.

Briz, of Madrid, has treated 38 cases of pertussis in children, two of whom were infants at the breast and the rest aged from 3 to 10 years, by inhalations of fluoric acid, 10 c.cm. of which were added to 250–300 gm. of water, and obtained a cure in eight to ten days.

Van der Starp records a case of pertussis complicated by bronchopneumonia successfully treated by subcutaneous injections of oxygen, as recommended by Naessens (vide *Medical Science*, 1921, **4**, 305).

Davison, of Baltimore, summing up the prolific and somewhat contradictory literature, concludes that injections of Bordet-Gengou bacillus vaccines may have a slight though unreliable prophylactic effect, and that therapeutic inoculations are of practically no value.

It has long been known that vaccination of children exposed to infection acts as a prophylactic against whooping-cough, Edward Jenner being the first to draw attention to the fact. Stern, of the Rostock University Children's Clinic, reports 20 cases of pertussis treated by the serum of recently vaccinated calves, a method which had first been recommended at the International Medical Congress at Moscow in 1897. The success of the treatment was remarkably striking, the attacks of coughing and vomiting being either stopped at once or rendered less frequent and intense, and the duration of the disease much shortened. 10 c.cm. were injected at

a time, and after two injections a distinctly curative effect was usually observed.

On the other hand, Bardach, of the Düsseldorf Children's Clinic, and Reiche, of the Hamburg-Barmbeck Hospital, report that the method entirely failed in their hands, neither the number and intensity of the attacks nor the course of the disease being in any way affected.

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J. D. R.

GONORRHOEA

Symptomatology. Sagot has collected the reports of 45 cases of *gonococcal endocarditis*, including one observed by himself and Hallé. Analysis of these cases shows that 31 occurred in males and 14 in females, including one child, aged 10 years, with vulvo-vaginitis. Arthritis was present in 26, and 40 cases were fatal. Gonococci were cultivated from the blood during life in 20 cases, and were found *post mortem* in the cardiac vegetations in 38 cases, either microscopically or by culture. In about one-third of the cases the aortic valves were affected. Sagot concludes that gonococcal endocarditis may be benign or vegetative; that the benign form is more common than is generally supposed, and is a probable cause of chronic cardiac disease; that the vegetative, or ulcerative, form has the characters of an acute septicaemia with cardiac symptoms and is usually fatal; that the danger of septicaemia increases with extension of the disease to the deeper genito-urinary organs, but bears no definite relation to the severity of the primary infection.

Rivaz reports a case of the rare complication of gonorrhoea, *keratodermia blenorrhagica*. The patient, a male, aged 25, when first seen, had acute gonorrhoeal urethritis, and had had a previous attack six months previously. He was treated with permanganate irrigations and a polyvalent vaccine. In the third week he suffered from pain in the knees and ankles, and ran an evening temperature: the prostate was found to be swollen. After temporary improvement effusion into the knee-joint occurred, and a nodular eruption appeared on the soles of the feet. The eruption spread to the dorsal surface of the toes, and in places was rupioid in appearance. A few days later the eruption appeared on the palms. The nodules increased in size, coalesced, and developed a cheesy core. In about a fortnight the epidermis peeled off in large flakes; the toe-nails were shed owing to accumulation of epithelium beneath them, but there was no loss of finger-nails. The condition cleared up about two months after its first appearance.

Citron reports a case of *gonococcal septicaemia* which was cured by subcutaneous injection of 50 c.cm. of meningococcal serum. The patient, a man aged 27, suffered from acute polyarthritis, chiefly affecting the right wrist and the left ankle-joint, raised temperature, and rigors. Examination of the urethra was negative, but a recent attack of gonorrhoea was admitted. All symptoms, including a systolic murmur at the apex, disappeared a fortnight after the injection. Local treatment was also carried out by daily irrigations into the bladder with permanganate of potassium and internal administration of salol. Citron refers to cases reported by other observers which benefited by meningococcal serum—acute gonorrhoeal affections of the internal genital organs in women by Le Masson, and

gonorrhoeal arthritis by Barbe, and concludes that this serum is indicated in all severe cases of general gonococcal infection.

Another case of *gonococcal septicaemia* is reported by Weill and Colaneri. In this case symptoms of septicaemia developed in a man during the acute stage of gonorrhoeal urethritis. There were no metastases and no arthritis. The gonococcus was cultivated from the blood on bouillon-ascites fluid and bouillon-hydrocele fluid. The patient died a month after symptoms of septicaemia commenced. Post-mortem examination showed septic pneumonia, but no gonorrhoeal lesions in the endocardium, kidneys, bladder, prostate, or seminal vesicles. Treatment by intramuscular injections of electrargol and afterwards by antimeningococcic serum and an autovaccine had no effect.

Valentin remarks on the frequency of relapses in *gonorrhoeal vulvo-vaginitis in children* after local treatment of the vagina and urethra only with injections of protargol. He therefore sought for the cause of the relapses in the para-urethral ducts, the bladder, the cervix, Bartholin's glands, and the rectum. Implication of the para-urethral ducts was found in only one case, and gonorrhoeal implication of the bladder, cervix, and Bartholin's glands was not found in any of his 161 cases. The chief source of relapse was found to be the rectum. In 61 children treated in the above way gonococci were found in the rectum from 6 to 21 weeks after apparent cure of the urethra and vagina. On the other hand, in 26 children in which no gonococci were found in the rectum during periods of observation lasting from 4 to 9 months there were no relapses.

Diagnosis. Norris and Mickelberg give an analysis of 794 examinations of films (Gram's) from women presenting clinical evidences of gonorrhoea. The conclusions may be summarized as follows: (1) Gonococci are easily found in the acute stage, with difficulty later. It is therefore important to confirm bacteriologically a clinical diagnosis of gonorrhoea as soon as possible. (2) The presence of gonococci can be demonstrated by film preparations from every case if a sufficient number of correctly performed examinations are made. Many examinations may be required, however (fifteen in some cases). (3) A single negative smear is without significance. The chances of finding gonococci in a film from a chronic case are about 3 or 5 to 1 against, according to the skill of the examiner. (4) Staining and examining films for gonococci is not 'anybody's job.' It needs an expert. (5) For practical purposes all suspicious cases should be regarded as gonococcal until proved otherwise. Clinical evidence is of greater value in diagnosis than staining methods, even when the latter are performed by an expert. The authors believe that the usefulness of staining methods in the diagnosis of gonorrhoea in women has been considerably overestimated.

Minor details of technique are the following: For collection of material, a medicine dropper drawn out in the flame to 6 or 8 c.cm. in length is advocated. A dry cotton swab enmeshes the solid particles of the discharge, i.e. those elements most likely to contain gonococci. A cotton swab wet with a solution of mercuric chloride is good; it should be rolled on the slide, not rubbed. The perchloride tends to fix the solid particles and facilitates staining. In vulvo-vaginitis of children, washings from the vagina are useful; they are obtained with a soft rubber eye syringe filled with weak mercuric chloride solution, which is repeatedly forced into the vagina and sucked out again; the solution is afterwards centrifuged at slow speed.

Prophylaxis. Schumacher prefers albargin to protargol, hegonon, or other silver preparations, as it contains a higher percentage of silver, and can, therefore, be used in weaker solution. A 1 per cent. solution is considered a sufficient prophylactic against the gonococcus. As in the case of mercury, solutions of the silver salts must contain silver ions in order to be effective. Schumacher points out that perchloride of mercury acts as a prophylactic against both the spirochaete and the gonococcus, and can hence be used alone. The chief objection to general use is its poisonous property. Schumacher, therefore, suggests the use of a 5 to 10 per cent. solution of albargin as a general prophylactic, and holds that the silver ions have also a bactericidal action against the spirochaete.

Treatment. Phélip claims good results from *silver ionization* in the early stages of gonorrhoeal urethritis. The salts used were a 1 per cent. solution of permanganate of silver, and, when acute inflammation was present, 3 per cent. protargol. After emptying the bladder and washing out the anterior urethra with warm sterile water, the urethra is anaesthetized with 5 c.cm. of 2 per cent. cocaine for 8 minutes; then 10 c.cm. of the silver solution are instilled. An ionizator with an olivary end, of size 13 Charrière, is then introduced and is connected with the negative pole, the positive pole being placed on the thigh. A current of 2 to 3 milliampères is passed for 3 to 5 minutes. At bedtime the patient washes out the urethra with weak permanganate solution, or oxycyanide of mercury if there are secondary micro-organisms. The ionization is repeated on the two following days. If gonococci continue in the secretion the treatment is repeated. By this method, according to Phélip, the discharge and gonococci disappear in an average of eight days, in cases where treatment is commenced before the tenth day. As regards the mode of action, he suggests that the bactericidal action may be due to the formation of nascent electrargol, and that exaltation of cellular diaphylaxis and also mechanical action on the obstructed glandular orifices may each play a part.

Haxthausen quotes the investigations of Eisenberg and Okolska (*Zentralbl. f. Bakt.* [*&c.*], 1st Abt. Orig. 1913, **69,** 312) as having shown that the action of certain disinfectants can be greatly increased by the addition of even small quantities of alcohol. He also suggests that in the case of gonorrhoea the low surface tension of alcohol may enable a disinfectant to penetrate further than a watery solution. He also notes the effect of a dilute solution of alcohol on the diffusion of certain drugs. On the strength of these considerations he has treated over 100 cases of acute uncomplicated and mild complicated cases of gonorrhoea in the male with a solution of *protargol* (0·5 per cent.) *and alcohol* (5 per cent.). He uses as a control Jersild's (*Ugesk. f. Læger.*, 1913, 961) report on 116 cases of gonorrhoea treated with a watery solution of protargol followed by a watery solution of silver nitrate later in the disease. Haxthausen finds the comparison favourable to his treatment, a considerable proportion of his early cases being cured in two or three weeks—a rate of recovery which he thinks is practically unattainable with other distinfectants. Fewer complications occurred during treatment among his than among Jersild's cases. But some of his uncomplicated cases were slow to react to his treatment, and he confesses that in such cases it may be advisable to resort to the old-fashioned silver nitrate irrigation.

In a subsequent paper Jersild, who has treated fourteen cases of gonorrhoea of the urethra in women and of vulvo-vaginitis in children with alcoholic solutions of protargol, and has compared the effects with those

obtained in twenty other cases treated with a watery solution of protargol, has nothing good to say of the former method. Its most notable characteristic being its expensiveness, he has abandoned it.

Mann advocates *acriflavin* for the irrigation treatment of gonorrhoea. He uses a 1 in 4,000 solution in normal saline once a day. In anterior urethritis, after irrigation, some of the solution is retained in the urethra for ten minutes. In total urethritis irrigation into the bladder is performed. Good results were obtained in thirty-six cases of acute and chronic urethritis.

Oettinger and Deguingand report on eight cases of gonorrhoeal arthritis treated with *antigonococcal serum*. The results obtained by intra-articular injection were much more rapid and effective than when the serum was injected subcutaneously.

Scherliess claims good results with *hot water irrigation* in gonorrhoea in soldiers, from an experience of about 200 cases. The apparatus he uses consists of an outer tube of the size No. 18 or 19 Charrière and 11 cm. in length, with several long windows, and an inner tube which is connected with the irrigator. The water passes from the inner tube to the outer, through the windows in the latter on to the mucous membrane, and escapes by the outer tube. The temperature of the water is at first 34° C., and is gradually raised by the addition of hot water to 48° C.; the duration of the irrigations being from 10 to 30 minutes, and the intervals between them six days. During the intervals injections of weak silver nitrate solution are given every other day. The author states that this method can be used in the most acute cases, and also when epididymitis is present, and that the hot water has a marked bactericidal action on the gonococci. In his 200 cases, Scherliess states that there were only three failures after the above treatment. Extension to the posterior urethra was rare, and when present is said to have subsided under the hot-water injections, which are adapted to the anterior urethra only.

Lindblad has tested the value of *milk injections* in gonorrhoeal diseases of the eyes by a statistical comparison of the results obtained at the Sabbatsberg Hospital before and after the introduction of this treatment, which, for the past year and nine months, had been adopted in every case of gonorrhoea of the eyes. Before this period, only local treatment had been given. The milk treatment, which was supplemented by ordinary local treatment, consisted of the intragluteal injection of 4 to 6 c.cm. of cow's milk boiled for 5 minutes. The comparison showed that, under local treatment only, adults lost their gonococci after an average period of 22 days, whereas adults treated with injections of milk lost their gonococci after an average period of 10 days. In the case of children, however, the results were slightly in favour of the patients not treated with milk, the average time taken in the disappearance of gonococci being between 7 and 8 days as compared with 10 days. In the case of the new-born, the injections seemed to do more harm than good. Lindblad concludes that this treatment is beneficial in some cases, but it does not deserve extravagant praise.

The effect of *antigonococcal serum* has been studied by experiments on the rabbit by Terrien, Debré, and Paraf. They found that injection of an emulsion of gonococci into the anterior chamber of the eye produced in 10 to 15 days irido-cyclitis with a marked tendency to the formation of synechiae and hypopyon. The injection of antigonococcal serum into the anterior chamber 24 hours after the gonococcal inoculation completely modified the evolution of the ophthalmia and cured the lesions in a few

days. Intramuscular, intravenous, and intraconjunctival injections of the serum, however, had no effect. Intra-ocular injections of antimeningococcal and antidiphtheritic serums were also inefficient. The authors are therefore of opinion that antigonococcal serum, to be effective, should be injected into the actual focus of disease. This, however, does not apply absolutely to the effects of serotherapy in the human subject, for in the case of the rabbit it was found that the gonococci did not multiply in the ocular lesions, and the action of the serum was only endotoxic. The serum used was Nicolle's, prepared at the Pasteur Institute.

Sagot regards subcutaneous or intravenous injection of antigonococcal serum as the most promising form of treatment in cases of gonococcal septicaemia. He mentions the experiments of Debré and Paraf with this serum in animals. Three monkeys injected intraspinally with a culture of gonococci all died, while three other monkeys, in which the injection of culture was followed by an injection of antigonococcal serum, recovered. Sagot mentions that, in the human subject, the best results have been obtained with large doses of the serum. Vaccines, which are often successful in the various complications of gonorrhoea, have little or no effect on severe gonococcal septicaemia with endocarditis. The same with antimeningococcal serum, which has given beneficial results in arthralgia, but not in severe arthritis or septicaemia. Antistreptococcal serum, which was found successful in two cases of gonococcal septicaemia by Parkinson and Fenwick (1906), was tried by Sagot with a negative result.

Reenstierna reports favourable results from the treatment of gonorrhoeal complications by a *combination of antigonococcus serum and a temperature-raising agent.* He first tried a polyvalent serum made by immunizing goats by intravenous injections of living gonococcal cultures. This serum gave a complement fixation and agglutination, and showed a protective influence against gonococcus toxins in experiments with guinea-pigs. In cases of urethritis, Bartholinitis, and conjunctivitis the serum had no effect in decreasing the gonococci, but in arthritis, epididymitis, prostatitis, and other complications of gonorrhoea the symptoms subsided in a few hours, and most cases, after repeated injections, were cured more or less rapidly. A few cases were refractory. More recently, Reenstierna has combined the serum with a substance which raises the patients' temperature. The gonococci are then attacked by two agents, antibodies and heat. For this purpose he added to the serum dead cultures of typhoid bacilli. With this preparation he has treated more than a hundred cases of gonorrhoeal complications, especially arthritis, epididymitis, and prostatitis. Cases of arthritis are said to have been cured after one or two injections. In many cases the serum caused immediate improvement after gonococcal vaccines had failed. Most cases of epididymitis and prostatitis were rapidly cured. A few cases resisted, possibly owing to secondary infection.

Sézary discusses the variable results of *antigonococcal vaccinotherapy.* He confines his remarks to stock vaccines, as autovaccines are often impossible to obtain. The antigen, he remarks, should be as little changed as possible, but this condition is difficult to realize, as the gonococcus undergoes lysis in cultures of 24 hours, and also when suspended in saline solution. Too prolonged heat also modifies the antigen. For these reasons the gonococci should be removed from culture after 18 hours and transferred to an oily medium, which does not cause lysis, and should be killed by cold instead of heat. In practice, subcutaneous injection of a therapeutic dose should

produce a febrile reaction, which is the only proof of its action. The lipovaccine has the advantage of introducing an increased quantity of antigen with only slight febrile reaction. The proper dose, according to Sézary, is that which will cause a slight febrile reaction of 38° to 38·5° C. Larger doses, he thinks, tend to produce complications, such as arthritis, owing to the production of an intense and prolonged negative phase. A febrile reaction should occur after each dose, which must be progressively increased as the organism becomes accustomed to the previous dose. An interval of 24 hours should elapse after the last reaction has subsided. Neglect of this rule retards cure by prolonging the negative phase. As a rule, Sézary injects every three days. With the lipovaccine 6 or 7 injections, representing 60 to 80 thousand millions of gonococci, are necessary. In some cases there is marked improvement the day after the first injection, which Sézary attributes to protein shock; but these cases often relapse afterwards. In conclusion, Sézary remarks that we must not expect too much from vaccinotherapy. Its rôle is to stimulate and reinforce the reaction of immunity; but this action may be slow and insufficient.

Boyd has investigated the value of vaccines in acute gonorrhoea. The vaccine used was a mixture of several strains of gonococci with several strains of staphylococci cultured from cases of gonorrhoea with mixed infection in the proportion of one part gonococci to three parts staphylococci. The gonococci were cultured on Thomson's glucose plasma agar, subcultured in the usual way, and standardized to 1,000 millions per cubic centimetre. From 6 to 12 strains of gonococci and staphylococci were used. The average course consisted of 1 c.cm. given at intervals of 3 or 4 days. Comparing 270 cases treated with vaccines with 200 control cases treated without them, it was found that the vaccine had no effect on the course of acute gonorrhoea.

Demonchy advocates the use of vaccines in acute gonorrhoeal urethritis. The doses should be small, to avoid severe reactions. He claims that doses of 1 to 5 mgm. of his vaccine, given at two or three day intervals, cause disappearance or attenuation of the pain and congestion after the first or second injection, and diminution of the discharge after the fifth or sixth. He considers that the cure depends less on the number of injections than on the total amount of antigen introduced, and that it does not usually take place till 4 cgm. have been given. Cases treated in the early stage with vaccines, combined with irrigation, were cured more rapidly than cases treated with irrigation only. In order to test how far the result was due to the general reaction he experimented with two series of patients, all with acute gonorrhoea. To one series a non-gonococcal vaccine was administered, to the other series a gonococcal vaccine. In the latter series the duration of the disease is said to have been reduced to six or eight days, but in the first series, injected with non-gonococcal vaccine, the discharge diminished for a day or two, but the duration of the disease was not shortened. When the specific and non-specific vaccines were administered during the period of decline of gonorrhoea, however, there were rapid cures in both instances. From this Demonchy concludes that vaccines have both a specific and a non-specific action. For the preparation of his vaccines he uses peptone agar, and claims to obtain good cultures without the addition of ascites fluid, blood, &c.

Cusson, from an experience of 22 cases of gonococcal epididymitis, concludes that intravenous injections of *antityphoid vaccine* give the best results. He thinks that the specificity of the vaccine plays only a secondary

part in the treatment of the complications of gonorrhoea, and that the therapeutic results are not proportional to the dose injected. He advises small doses repeated not later than five or six days.

Weill reports favourable results from the *subcutaneous injection of hydrocele fluid* in cases of gonococcal epididymitis complicated with hydrocele. He reports three cases, in the first of which two injections of 10 c.cm. were given, in the second one of 5 c.cm., and in the third one of 3 c.cm. The first case improved most rapidly, and Weill considers that the therapeutic effect is proportional to the quantity of liquid injected. There were no general or local reactions. The fluid was heated to 45° C. before injection to destroy any possible gonococci. Weill calls this procedure auto-plasmotherapy, and mentions that beneficial results from this method were published some years ago by Marinesco. Weill also obtained improvement in two other cases of gonorrhoeal epididymitis by injections of hydrocele fluid from the first case—hetero-plasmotherapy.

Cumming and Glenn recommend *vas puncture and injection of collargol* in cases of acute and chronic seminal vesiculitis. Puncture is best done midway between the epididymis and the external ring. After local anaesthesia a small incision is made in the anterior surface of the scrotum, the cord is exposed, and the vas isolated by stripping its coverings longitudinally. The vas is held by a piece of gauze and a hypodermic needle containing a horsehair is inserted. The horsehair can be seen within the lumen of the vas. The horsehair is withdrawn and a little water injected; if this passes easily, the medicinal solution is injected: 20 c.cm. into each vas followed by a little water. There is no means of judging how much of the solution passes directly into the bladder without first passing through the seminal vesicles. The solution used was collargol, 5 to 10 per cent. in most cases; mercurochrome and cargentos in a few. The extent of injection of the vesicles is shown by skiagrams. Before these are done the patient empties the bladder, and this is then distended with air.

As the result of an experience with 55 cases the authors conclude that this is an effectual method of treatment of gonorrhoeal infection of the seminal vesicles; that, while not a certain cure, it leads to improvement in most cases, and to cure in some; that it should be combined with the usual treatment for associated conditions of urethritis and prostatitis; that vas puncture is contra-indicated in cases with acute anterior urethritis or acute epididymitis. In five of their cases active spermatozoa were found in the secretion obtained by prostatic massage.

Tests for cure of gonorrhoea. Fraser remarks that while some standards of cure are too low, others are so high that they defeat their own ends. He warns against over-treatment and over-instrumentation, which damage the urethral mucous membrane and render it vulnerable to further infection by gonococci or secondary organisms. A standard of cure which is too stringent may lead to introspective neurasthenia. The following is the scheme advised by Fraser:

1. Clinical symptoms being absent after examination of the prostate, seminal vesicles, testicles, and perinaeum, and the urine being clear and the urethra easily dilated, the patient is kept under observation for twelve days, during which he takes vigorous exercise. This should cause no return of urethral discharge and the urine should remain clear. The presence of a few filaments may be disregarded, if these are free from pus and micro-organisms.

2. A provocative injection of polyvalent gonococcal vaccine (100 millions) should cause no reaction.

3. Massage of the urethra over a curved sound should produce no pus.

4. In three months, and again in six months, the patient should be re-examined—by the two-glass test, massage of the prostate and seminal vesicles, general clinical examination, and examination of the whole urethra, either by olivary bougie or urethroscope. Urethroscopic examination performed directly after cessation of symptoms is of no value, as the urethra has not had time to return to normal, and may also be detrimental by damaging the mucous membrane. The proper time is after three months' interval, when the mucous membrane should appear of uniform colour, reflecting light equally, with uniform and well-defined folds, responding uniformly to air dilatation. Slowness of dilatation, the presence of hyperaemic patches, and inflammatory signs round the openings of the glands of Littré and lacunae indicate further treatment.

Fraser concludes that there is no absolutely certain test for cure, but considers the above programme practical and sufficient. It avoids the risk of over-treatment and thereby removes much of the possibility of perpetuating the life of the gonococcus, of permanently damaging the urethra, of causing local and metastatic complications, and of making the patient a neurasthenic. He warns against too energetic hunting for gonococci by means of platinum loops, which may damage the urethra. The gonococcus, indeed, may, after a time, become saprophytic and non-pathogenic. Clinical observation is more important than perpetual search for gonococci.

With regard to the complement-fixation test, he thinks that more knowledge of the different types of gonococci and a more sensitive antigen are required before the test can be rendered reliable. Again, urethritis limited to the anterior urethra usually gives a negative result, and the same result may be due to incarcerated foci of gonococci producing no demonstrable antibodies. It also appears that the production of antibodies continues for a considerable time after destruction of the gonococci. Hence, the only criterion of cure is change from positive to negative after an interval of about three months. In cases treated with vaccines, especially detoxicated vaccines, the artificial immunity induced renders the test inapplicable. On the whole, therefore, the test is, at present, unreliable.

Volarelli, who has investigated the tests for cure of gonorrhoea from the results of 172 cases, considers that the best test consists in provocative injections of gonococcal vaccine, together with bacteriological and cytological examination of the secretion. He finds that, in cases with urethral secretion and filaments in the urine but no demonstrable gonococci, provocative vaccine injection produces increased secretion with gonococci in 47 per cent.; also that the secretion shows cytological modifications which furnish diagnostic evidence in the absence of gonococci. The chief of these is the presence of numerous polynuclear leucocytes, which he regards as indicating the presence of active infection. These were frequently present in cases which were negative for gonococci. Preponderance of epithelial cells over leucocytes indicates that the infection is subsiding, and absence of leucocytes after provocative injection signifies a cure. In most of his cases two intramuscular injections of 50 million and 100 million were given with one day's interval; sometimes a third injection of 150 million. In some cases the vaccine was administered intravenously in a single dose of 1 c.cm., but no

appreciable difference resulted from this method, except that the effect was more rapid.

Herrold has attempted to establish a more definite standard of cure in gonorrhoeal infections in the male by improved methods for cultivation of the gonococcus, and by study of the value of provocative and serological tests. He concludes that cultures of prostatic and seminal secretions and the first urine sediment furnish the most reliable means of determining whether a gonorrhoea is cured. For this purpose he uses phosphate agar with blood and ascites fluid as the medium, and inoculated plates incubated under reduced oxygen tension. He regards the complement-fixation test as a valuable aid when taken in conjunction with the cultural results. A low degree of positive fixation may persist, according to Herrold, for longer than is usually stated—up to a year after smears and cultures are negative. The precipitin test he regards as less sensitive, but because of its greater simplicity it may be used as a substitute for complement fixation. He has found no advantage from the use of provocative tests, either urethral injection of silver nitrate solution or subcutaneous injection of gonococcal vaccines, before taking cultures or smears. He considers it a fallacy to regard the presence or absence of pus in the secretion as an index of cure, for in 30 cases with negative cultures and negative fixation tests pus cells were present in the smears in more than half. Many specimens of urine with filaments proved negative to culture.

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C. F. M.
A. E. Q.
C. L.

DISEASES OF THE SKIN

Perhaps the most important event in the dermatological world during recent months has been the formation of the British Dermatological Association, which is to be strictly confined to those who are really interested in the subject. The first meeting, which was very successful, was held in London on November 18. A number of striking cases were shown, and discussions were held on 'Focal infections' and the 'Value of the Wassermann reaction as a guide to treatment'.

The output of dermatological work has been well maintained during the past months. As far as possible it will be classified according to subjects, but much of it consists in the study of isolated cases which are difficult to group together.

The connexion between skin disease and internal disorders. This subject has attracted a good deal of attention. A discussion was opened on it at the Medical Society by Sir James Galloway in a learned paper, and subsequent speakers took up the question from different points of view. Barber laid great emphasis on focal infection and ascribes a number of

different dermatoses, e.g. alopecia areata, lupus erythematosus, erythema multiforme, &c., all to this cause. Leslie Roberts has also written on focal infection, but he is not so enthusiastic about it as Barber.

In America the theory of protein sensitization as a cause of various dermatoses has been most popular. Towle regards it as an accepted fact, but admits that much work remains to be done before full use can be made of it. Highman and Michael consider it has something to do with urticaria, and that search should be made for offending articles of diet. In France, Vidal draws attention to the connexion between urticaria and anaphylaxis and treats urticaria by giving a dose of peptone an hour before meals. All these writers admit occasional failures.

Pignet reports a case of what he calls 'anaphylactic' urticaria, occurring after the sixteenth injection of a dose of calcium potassium manganate, the trade name of which is 'bactioxyne'.

Tuberculosis of the skin. A discussion on this subject was held by the British Medical Association, and most of the speakers arrived at the conclusion that few sufferers from lupus contracted visceral tuberculosis. This is perhaps contrary to what one would have expected.

With has made an exhaustive investigation as to the frequency with which various localities are attacked by lupus. He has analysed 900 cases and confirms the old observation that lupus most frequently attacks the nose, but he states that it is comparatively unusual either on or in the nose in young children, but becomes much more common in that situation between the ages of 11 and 16. He also notes that lupus not infrequently attacks the extremities during childhood. Parkes Weber (1) publishes an interesting case of symmetrical ulceration of the extremities in a young child, somewhat resembling lupus pernio, associated with extreme redness of the cheeks. Ravaut (1) claims to have cured a case of lupus of the cheek of twelve years' standing with a single application of diathermy. The presentation of this case to the French Dermatological Society was followed by an interesting discussion on Finsen-light treatment. The speakers with one exception deplored the poor results obtained in France compared with Germany and the Scandinavian countries. The necessity for unremitting care and attention in the application of the Finsen light was emphasized, and the tiring nature of the work. Friedmann's vaccine was condemned by Buschke.

Ringworm. The most important work on this subject is a paper by Bloch, who has tried to show that there are conditions which he calls trichophytides, eruptions which bear the same relation to trichophytic infection proper as tuberculides bear to tubercle. He describes three forms which he considers common: (1) a nodular, (2) a lichenoid, (3) a scarlatiniform erythema. In discussing the pathogenesis of these lesions he states that an allergy of pronounced type must be present, and he considers that they are allergic reactions of the skin to the presence of fungi or their toxins. The diffusion of the toxin takes place by the blood. He has sometimes been able to produce them by the injection of trichophytins into the veins. Bloch's observations have been confirmed by Williams in America, who has described four cases of lichenoid trichophytides in patients suffering from severe ringworm. Possibly these eruptions are commoner than has been supposed.

Weidman and McMillan call attention to the necessity of standardizing the culture media used for growing parasitic fungi in view of the variations

caused in the appearance of the cultures by modifications in the medium. They point out that Sabouraud's original maltose was an extremely crude product, and now that no more of it can be obtained they recommend that a common formula be used by all workers on the subject, employing pure chemicals and Chassaing's peptone. Lombardo has studied the production of pigment in those cases where a pigmentation of the skin is produced, and comes to the conclusion that the pigmentation found in various trichophytic infections and in pityriasis versicolor is due to the pigment formed by the fungus itself, not to pigment formed in the skin. Writing on ringworm of the beard, Veilchenblau points out that a source of infection not often considered is the towel which is used by the barber to encircle the patient's neck and head. Escomel describes a case of ulceration of the foot from Peru which was due to a discomycosis.

Scabies. Dyson has studied camel itch, an irritating eruption caused in camels by an acarus which is capable of being transmitted to man, but which soon dies and cannot propagate itself on the human subject. Thibierge and Stiassnie have found that practically the same thing is true of feline scabies. The treatment of scabies by the soluble compounds of sulphur, notably the polysulphides, as is shown by Petges, finds several supporters on the Continent, who claim for it far greater speed than the older method of *frottement*.

Psoriasis is not very conspicuous at present, but Small has published a series of cases to show the incidence of trauma upon its development, while Remer and Witherbee advocate the extensive use of X-rays in its treatment, even when it is widely spread. They claim results at least equal to those of any other method of treatment.

Ichthyosis. Several papers have appeared on this subject. Golay publishes an interesting case of diffuse congenital hyperkeratosis, fatal at 7 months of age. This was the seventh child of the mother, three of whose previous children had died of the same condition, all after she had gratified an abnormal desire for salt during her pregnancy. Heller also publishes a case illustrating the familial influence in ichthyosis. He found three different families in which during three generations no less than 50 per cent. of the members were affected. Manson also publishes three cases of ichthyosis follicularis in one family.

Exotic skin diseases. Clement, Donato, and Paret publish an interesting study of granuloma tropicum, of which they saw many examples in the military hospital at Marseilles. It is a cutaneous fuso-spirillosis, giving rise to a transitory Wassermann reaction and is easily curable with curettage and iodine vapour. Tamura publishes a full description of creeping disease, with a parasite which he identifies as a gnathostoma in his case: previously the larva of the gastrophilus fly had been thought to be the cause. Ketron cures larva migrans by application of carbon-dioxide snow. Ravaut (2) publishes two cases of oriental sore in soldiers who had never been to the East.

Interesting cases of **traumatic dermatitis** are reported (1) by Kall, contracted by using a new alpenstock; and (2) by Frei, a matchbox dermatitis caused by carrying in the trouser pocket a matchbox coated with phosphorus sesquisulphide. McCord and Kilker describe zinc chloride poisoning, an industrial disease which causes in workers lesions very similar to chrome sores. MacKee and Andrews discuss radium and X-ray dermatitis, and conclude they are essentially the same.

Septic infections. Jacobs gives a full study of a case of *human glanders* occurring in a farmer, which, however, was only diagnosed after death. Plaut describes two cases of *noma* occurring in the course of an epidemic of influenza, both associated with profuse infection by spirochaetal organisms. One case he cured with salvarsan, the other was already moribund when first seen. Montgomery and Culver discuss *streptodermatitis* in its relationship to wounds. They describe it as an infective disease spreading with an advancing margin like erysipelas. They recommend treatment with weak lead acetate lotion or copper sulphate. Chipman also discusses streptococcic infections chiefly in relationship with eczematization. Under this head may perhaps also be mentioned a case of *subacute malignant pemphigus* (Lane and Lambert) which terminated fatally after three months.

Seborrhoea has been studied by Cumston, who divides the disease into two stages : the first, thickening of the sebum ; the second, inflammatory in type. Unna claims rosacea as a manifestation of seborrhoeic eczema.

New growths of the skin. Kingery has done some interesting work on the aetiology of *common warts*. He finds that an extract of warts passed through a Berkefeld filter and injected subcutaneously causes the production of warts after an incubation period of four to six weeks. These fresh lesions can again be extracted in the same way and the extract again produces the same effect on injection. Lespinne publishes a full study of an extensive case of *zoniform naevus* which caused marked hypertrophy of the side of the body affected. Radvin publishes a typical case of *xerodermia pigmentosa* with pigmentation present from birth, which terminated fatally notwithstanding treatment by X-rays and radium. Hamilton publishes a case of a woman who developed *epithelioma* after taking Fowler's solution for psoriasis for a period of thirty-six years. For twenty years of the time she had shown arsenical hyperkeratosis. Levin discusses *von Recklinghausen's disease*, and comes to the conclusion that it is essentially an ' endocrine dysfunction '. If not anticipated by some intercurrent condition it may cause death by progressive asthenia. Finnerud describes a severe case of the *sarcoid of the Boeck-Darier-Roussy type*. Under this head may perhaps also be mentioned a study of the rare condition known as *pseudoxanthoma elasticum*, only fifteen cases of which have been published altogether. Sequeira has described at some length a case of the ' precancerous *dermatosis of Bowen* ', the first which has been diagnosed in this country.

Fox reports a case of Hodgkin's disease with *lymphogranulomatosis of the skin*. He thinks that Hodgkin's disease bears no relation to tuberculosis, but that mycosis fungoides may possibly be a cutaneous manifestation of lymphadenoma. A similar case is described by Butler of lymphatic leukaemia, in which the first manifestation of the disease was the development of skin tumours.

Certain isolated cases deserve mention. A case of *porokeratosis* is described by Wright in some detail. His case was associated with much pruritus, a rare concomitant of this condition. Is it possible it was a form of lichen annularis ? The illustrations suggest this possibility.

Synovial lesions of the skin are investigated by MacKee and Andrews. They consist of small globular projections occurring over the skin of the finger-joints. They may be treated either by excision, X-rays, or radium.

Parkes Weber (2) publishes an interesting case of *pseudo-icteric xan-*

thosis in a man who had been yellow since birth but otherwise healthy. He regards it as a case of xanthaemia, but had had no spectroscopic examination made.

A case of *urticaria pigmentosa* occurring in an adult is reported by Wallace Beatty.

Chatellier describes a curious case of a *recurring eruption of a vesicular character* in a young man with evidence of an hereditary predisposition on the maternal side. The remarkable point about the case was that although there was no eosinophilia in the blood the cerebrospinal fluid showed marked lymphocytosis.

Nicolas and his collaborators report cases of regrettable incidents after the administration of arsenobenzol; one was a case of Raynaud's disease with gangrene, the other pemphigus foliaceus.

Christopherson again reports that leucodermia may arise after the administration of antimony. He quotes the case of an Arab boy under treatment for bilharziosis. The leucodermia ultimately disappeared everywhere except on the lips, which remained a brilliant pink instead of a dull red. The Arab youth did not appreciate this change in pigmentation.

Apropos of the recent discussion on the relationship between herpes zoster and varicella and its infectivity, it is interesting to note that Fuhlrott reports an *outbreak of herpes zoster* in a camp of prisoners of war at Marseilles, where he was in 1916. Among 1,200 men there were ten cases, five of them from one barrack. Those who did not live in the same barrack had opportunities of mixing with the others at work and meals.

Morse reports a curious case of *calcification of skin* in a child. It does not appear to be a case of sclerodermia, but rather of a perivascular deposit of lime salts.

Treatment. Some progress has been made in the treatment of leprosy by the derivatives from chaulmoogra oil, i.e. gynocardic and hydnocarpic acids; work on this subject has been published by Sir Leonard Rogers and also by de Mello. de Mello has also found useful the oil of nim, derived from a plant which has been used by the Hindoos for ages.

Brenning has cured pemphigus by the injection of turpentine. Nicolas and Dupasquier have cured two cases of rebellious prurigo by injecting the patient's own serum into his tissues. Luithlen also recommends the same methods for severe pruritus, eczema, and acne.

Autovaccines still find supporters in Renaud-Badet, who uses them for sycosis, and Hilgermann for eczema. A rather novel form of treatment in dermatological practice is the filiform douche, which consists of water driven forcibly through a small aperture, 0·5 mm. to 1·5 mm. in diameter. Veyriers and Desaux recommend this for pruritus vulvae, lichen planus, and chronic lupus erythematosus. Pautrier has been able to devise a sulphur oil which is sufficiently non-irritating to be used for intramuscular injection; he finds it useful for psoriasis, acne, and alopecia areata. Sabouraud has written a practical article on the treatment of alopecia areata, the chief point in which is, that in children and adolescents he regards and treats it as a larval form of congenital syphilis. The French dermatologists are busy in devising metal applicators for the better and more delicate use of carbon-dioxide snow. Lortat-Jacob, and now Vignat, have invented special instruments for the purpose. Cacodylate of soda also maintains its popularity in France as a drug for intravenous and intramuscular injection. Cheinisse finds it useful in eczema, psoriasis, and some forms of prurigo. But he does

not like it in syphilis. McNair has reviewed at great length the remedies used for rhus dermatitis; the only remedy which he finds of any use is castor oil, which destroys the poison *in vitro* and is useful as a dressing.

Katzenstein advocates the use of arsenic for chronic erythema exudatiorum multiforme. He had one case which he was able to cure by arsenic administered *per os*, and a second which, having resisted this method, yielded to salvarsan.

Kissmeyer states that for more than a year the Finsen Institute in Copenhagen has been using trypaflavin with steadily increasing frequency and gratifying results. The chief indications are suppurating conditions of the skin, such as sycosis barbae, folliculitis, small perifollicular abscesses, boils, Bockhart's impetigo, impetigo contagiosa, and more deep-seated conditions, such as seborrhoeic abscesses in the axilla, and secondary infections, such as those commonly seen in varicose ulcers. Trypaflavin is also extensively used in weeping eczema, and after operations it is the rule at the Finsen Institute to paint the skin with trypaflavin dissolved in alcohol as a preventive of infection, the wound being covered with 1 per cent. trypaflavin gauze. Trypaflavin-dermophil (2 per cent.) has taken the place of zinc ointment as a covering for the skin after the Finsen treatment of lupus has provoked a severe reaction. The Finsen Institute has also used the English preparation proflavin, and has obtained the same results with it as with Casella's trypaflavin, which is used in both alcoholic and aqueous solutions as well as in ointment form.

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H. D.
C. L.

ABSTRACTS

SURGERY

Sargent, Percy. Lesions of the brachial plexus associated with rudimentary ribs [B.]. *Brain*, 1921, **44**, 95–125.

Percy Sargent discusses the conclusions that he has formed in operating upon 65 patients for cervical rib. He points out that the recognition of their neurological significance is of comparatively recent date, in spite of the fact that the presence of occasional abnormal rib arrangements was well known. Probably many cases classed in the past under the headings of brachial neuritis, brachial neuralgia, uniradicular palsy, progressive muscular atrophy, occupational palsies, and symmetrical atrophy of the hands were in reality due to rib abnormalities; e.g. four out of six cases of uniradicular palsy recorded by Buzzard in 1902 as instances probably owe their symptoms to the presence of cervical rib; Lewis Jones reviewed in 1908 a group of cases that he had described in 1893 as symmetrical atrophy of the hands in young people, and found cervical ribs to exist in ten out of the fourteen patients.

Relations between costal anomalies and the nerves constituting the brachial plexus. Sargent agrees with Wingate Todd that cervical ribs may be associated with normal constitution of the plexus. But he quotes dissections of Lucas, Herstlet, and Keith and a case of Arbuthnot Lane, in addition to several of his own, that tend to show that, as a general rule, Wood Jones's suggestion is correct—that cervical ribs are usually associated with some pre-fixation of the plexus, and abnormal 1st thoracic ribs with some degree of post-fixation; but the relationship is by no means constant.

Classification. Sargent quotes Gruber's classification as given by Keen, but points out that it fails to take note of presence or absence of articulation between the rib and the C. VII vertebra or of the direction or mobility of the rib.

He, therefore, proposes the following classification:

Type I. Exaggerated costal process of C. VII, not jointed, continued forwards and downwards, usually fibrous, and attached to 1st thoracic rib behind the scalene tubercle.

This type is the one that most commonly requires surgical intervention; it may not be very obvious in a radiogram.

Type II. Short rib, articulated to C. VII by costo-central and costo-transverse joints—continued as fibrous band to 1st thoracic rib as in Type I.

Type III. Jointed rib long enough to carry C. VIII root on its bony portion—attached by fibrous band to 1st rib.

Type IV. Jointed rib whose anterior end reaches the 1st thoracic rib and is either fused with it or has an articulation with it.

Type V. Rudimentary 1st thoracic rib, the anterior fibrous portion of which is attached to the sternum, usually by a rudimentary costal cartilage.

Relationship of spinal nerve to cervical ribs. The author finds that the commonest arrangement is that the 7th root lies on the bony part of the cervical rib and the 8th root (or the lowest cord) lies on the fibrous portion. Usually in these cases he has observed that the 1st thoracic nerve to the plexus is small or even absent; but occasionally it may be of good size; this conforms with the idea that cervical rib tends to be associated with a pre-fixed plexus. But no statement can be made that good development of the cervical rib implies more pre-fixation of the plexus, or vice versa.

Rudimentary 1st thoracic rib is a much rarer anomaly than cervical rib; this harmonizes with Wilfred Harris's statement that post-fixation of the plexus is less common in man than pre-fixation.

The sympathetic nerves. Main sympathetic nerve supply to upper limb comes from inferior cervical and 1st thoracic ganglion usually via 1st thoracic and VIII C.N. Percy Sargent has seen only one case in which there were oculo-pupillary signs; Thorburn had seen none.

Subclavian vessels. He confirms Todd by finding the subclavian artery either lying on 1st thoracic rib or just held off from it by the fibrous band—he saw no cases in which it passed over the accessory rib, though such a position has been recorded. Absence or diminution of the radial pulse when the arm hung dependent was a common phenomenon; dilatation of the artery in the region of the cervical rib was present to some extent in two of his cases, but none had the very definite aneurysmal dilatation recorded by some authors. But a systolic murmur, not conducted down the arm, was heard in several cases just above the clavicle, and it was found that its intensity could be made to vary with the position of the arm. He had no cases with arterial thrombosis or gangrene of the fingers, as described by Keen.

In Sargent's group all 'vascular symptoms' were attributable to vasomotor disturbances. As is usual, the subclavian vein escaped pressure.

Causation of symptoms. The onset of symptoms may be sudden and follow some definite strain, or it may be gradual; in the latter case the author believes the symptoms to be due to continued friction of the nerves against the non-ossified costal process, caused by arm and respiratory movements; he has frequently demonstrated during operation that in such movements the nerve is raised and rolled over; excision of the fibrous band relieves the tension on the nerve.

Sargent agrees with Thomas and Cushing (1903) in believing that the damage is attributable less to the bony prominence than to the fibrous band which extends from the costal process of C. VII vert., usually to the upper surface of the 1st thoracic rib, behind the axis of movement of that rib: in inspiration the anterior end of the 1st thoracic rib rises, its posterior part tends to sink, and so this band is rendered more taut and presses upon the adjacent nerve.

The age and sex incidences of this group of cases agreed with those of other observers. In 62 cases the average age was 35; 55 of these patients were female and 7 male; the youngest were 12, 13, and 15 years of age.

Symptomatology. He groups the symptoms under three headings according to whether they were due to damage of the (1) somatic afferent fibres (e. g. neuralgia, cutaneous and deep sensory disturbances); (2) somatic efferent fibres (e. g. muscular weakness, wasting, and electrical changes); (3) sympathetic fibres (e. g. circulatory disturbances, coldness, cyanosis, oedema, and certain paraesthesiae—tingling, numbness, feelings of coldness or swelling).

Counting each case with bilateral symptoms as two, the symptoms that led the patient to seek advice were as follows:

1. Weakness 79 per cent. (or clumsiness on fine movements).
2. Aching or paroxysmal pain 72 per cent.
3. Paraesthesia 39 per cent.

Muscular wasting was evident in 72 per cent.
Objective sensory loss in 34 per cent.
Vasomotor disturbance (signs) in 12 per cent.

The affected muscles. In the 32 cases belonging to Types I and II that showed muscular wasting the muscles affected were:

All intrinsic muscles of hand and superficial flexors of forearm	= 6
All intrinsic hand muscles (without forearm flexors) . .	= 14
Abductor and opponens pollicis	= 12
	32

Twelve therefore exhibited the peculiar localization in abductor brevis and opponens pollicis first described by Kinneir Wilson.

The sensory changes. The author gives a table showing the exact areas affected. In 60 per cent. of his cases there was no alteration of sensibility either to cotton-wool or to pinprick; in the others there was dullness over some part of the forearm and hand.

Pressure signs due to 1st thoracic rib. Edwin Bramwell, in 1903, suggested that pressure signs are sometimes due to a 1st thoracic rib and not to a cervical rib. Since then the condition has been well recognized, and has been operated upon by Stiles, Morley, Murphy, Stopford, Taylor, &c.

Treatment. The reader is reminded that cervical ribs are common without causing any symptoms; also that other causes may give rise to symptoms very like those of cervical rib, e. g. syringomyelia, progressive muscular atrophy, toxic neuritis. Minor treatment sometimes avails, e. g. change of occupation, greater use of other arm, use of a sling, development of muscles of the shoulder by exercises and massage. But operation is required for many cases; its object is not merely to remove an abnormal bone, but to divide or excise any non-osseous fibrous structure against which the nerves are being damaged. For example, in one case a clean subperiosteal removal gave no relief, but subsequent resection of the periosteum immediately abolished the symptoms.

Results of operation. In only two cases were there any untoward sequelae, viz.: (1) a severe organic monoplegia, which cleared up after many months; (2) an hysterical paralysis. There were no fatalities. Pain is generally relieved; of 27 cases, followed long enough to judge the result, 19 had no pain and 8 were considerably relieved. Vasomotor symptoms are relieved immediately in many; in others they completely or partly clear up after months or even years. The muscular wasting had been pronounced in 31 out of 50 cases; of these 12 have recovered as regards bulk

and strength, in 12 recovery is incomplete, in 7 there is no improvement; Sargent therefore gives a better prognosis as regards return of wasted muscles than Thorburn did in 1913 (*Proc. Roy. Soc. Med.*).

The article is well-illustrated and has a good bibliography. C. C. C.

Albanese, A. [Sulle modificazioni dei nervi trapiantati e sulle reazioni istologiche che essi provocano nell' organismo dell' ospite. [**On modifications in transplanted nerves and on the histological reactions excited in the tissues of the host.**] *Arch. ital. di chir.*, 1921, **4**, 215.

An experimental inquiry on the fate of nerve fragments transplanted into muscle, and on the differences in tissue-reaction in the host induced by homo-, auto-, and hetero-transplants. The animals used were rabbits and dogs. The nerves were implanted, with all precautions and great delicacy, into the glutei; there was no attempt to bring the grafts into relation with nerve cords. In the case of hetero-transplants the lipoids of the medullary sheath are slowly transformed into neutral fats; there is a rapid oedematous swelling of the axis cylinders, which persist nevertheless, though of necrotic aspect. The nuclei of the sheath of Schwann disappear though an ill-staining filamentous mass remains. The tissues of the host betray but feeble proliferation, with little tendency to invade the transplanted fragment. Homo- and auto-transplants alike show an intense transformation of lipoids to neutral fats which undergo rapid absorption. The axis cylinders quickly disappear. The sheath of Schwann preserves its appearance as an organized tissue even after 40 days, and the nuclei survive. At the same time there is a rich proliferation of the connective tissue of the host, with swift invasion and organization of the graft. E. R. C.

De Gaetano, L. Deformità del collo per malformazioni embrionali. Cisti e fistole congenite. [**Malformation deformities of the neck; congenital cysts and fistulae.**] *Arch. ital. di chir.*, 1921 **4**, 265.

Professor de Gaetano bases his review of the question on the study of 20 personal cases. He insists on the importance of serial sections for the elucidation of the true origin of many cysts and fistulae since only in three or four out of some hundreds of sections may the characteristic structures be found. He gives a new classification, or rather dual grouping, the one clinical, the other histological. The former, purely topographical and zonular is into (1) suprahyoid, or from the floor of the mouth; (2) thyrohyoid, having origin in the zone between hyoid and thyroid; (3) thyroid—at the level of that structure; (4) infrathyroid—in the zone between that organ and the sternum. The histological classification is as follows:

1st. Branchial (lateral, rarely median, with a tendency to lateralization).	(*a*) With 'ectodermal' type of epithelium (dermoid cysts).	A. Ciliated columnar epithelium (embryonic pharyngeal type)..
	(*b*) With endodermal type of epithelium (mucoid cysts) rich in lymphogenous tissue.	
	(*c*) Mixed epithelium; ectodermal with endodermal, either columnar or stratified.	B. Stratified epithelium (adult pharyngeal type.)
2nd. Thyro-glossal tract (median).	With columnar, or ciliated columnar cells, and nests of thyroid tissue at the periphery (from median-lobe bud).	
3rd. Thyro-pharyngeal duct (lateral and median).	(*a*) Thyroid, with thyroidal cells of embryonic or adult type (from lateral-lobe buds).	
	(*b*) Parathyroids (from parathyroid buds) (rare).	

He discusses other classifications and reviews the classical descriptions of His of the appearance and transformation of the branchial arches and sulci and the origin of the tongue, thyroid, and thymus in the human embryo, with the more recent modifications or amplifications due to Hammar. His own cases are well illustrated by numerous micro-photographs. The point of practical importance to the surgeon that the author brings out is that fistulae and cysts should be removed, not only entire, but with an ample margin of tissue immediately surrounding, since here are to be found the potential sources of further formations. E. R. C.

Berner, J. Smaa kjætterier om kræft. [**Small cancer heresies.**] *Norsk Mag. f. Lægevidensk.*, 1922, **83**, 152.

Is, Berner asks, the apparent decline of the incidence of cancer in old age due to an actual decline or to the comparative frequency with which the disease is overlooked in advanced old age? The investigations, which pointed to the second explanation being the correct one, were made at Ullevaal Hospital, where the records of the necropsies made in the 10-year period 1909–1918 were studied, and all the records of 710 necropsies at which cancer was found were scrutinized. These cases included not only those in which the cancer had contributed more or less to the cause of death, but also those in which there had been no signs of malignant disease, and the causes of death had been various acute or chronic diseases. In as many as 113, or 15·9 per cent. of the total, the clinical diagnosis of cancer had not been made, and in 29·3 per cent. of these cases the cause of death had been stated to be 'debilitas senilis'. Of all the necropsies on the subjects of cancer, 56 concerned persons over the age of 80, and about half this number (46·4 per cent.) were made on cases which had not been identified as malignant before death. But among the 229 necropsies on persons under the age of 60 the malignant character of the disease had seldom been overlooked before death (only in 7·4 per cent.). Berner concludes that, as in hospital practice about half the cases of malignant disease are not recognized as such before the death of very old persons, the frequency with which cancer is overlooked in such persons in general practice must indeed be great. C. L.

Brackett, E. G., Baer, W. S., Rugh, J. T. Report of the Commission to investigate the results of ankylosing operations on the spine. *J. Orthop. Surg.*, 1921, **3**, 515.

No differentiation is made between results of the two principal methods in use, fusion and inlay graft. Report is based only on facts obtained by personal examination of patients and of radiograms by members of the Commission. Records by individual surgeons are, on the average, imperfect, and they are not adequate for the purpose of the inquiry. In considering the influence of the operations, no distinction is made between the results of operative procedure and those of the mechanical fixation instituted afterwards.

Influence on the subsequent development of deformity. Ankylosing operations cannot be depended upon to prevent the increase of deformity or of destruction of vertebrae. Deformity is always proportional to the destruction of the bodies of the vertebrae. Cases in which prolonged

mechanical treatment has followed operation have shown a markedly smaller degree of deformity than those in which mechanical treatment was abandoned early. This is particularly true of children. Operations also do not protect the patient from the effects of strain on the back. Fusions and inlay grafts can fracture or bend. After fracture of a graft acute symptoms have usually reappeared. This demonstrates the value of a graft and suggests that the graft should be large and firm.

Ankylosis of the operative field cannot be determined by X-ray examination. Ankylosis was tested by physical examination. It occurred in 85 per cent. of cases. The older the patient the greater the probability of ankylosis.

Fusion of the bodies of the vertebrae. Operation has little influence on this. All fusions of the bodies seen were in young subjects who were examined 4 or 5 years after the date of the first X-ray examination. No case of fusion was seen in an adult.

Influence of the operation upon acute symptoms. Operation undoubtedly exerts a beneficial influence on acute symptoms even where imperfect mechanical support, or ambulatory treatment, is used.

Abscess and paralysis were both too uncommon to give sufficient data for an opinion. Probably operation has a favourable effect, due in part to the enforced prolonged recumbency.

Mortality. Immediate mortality is low and infection rare.

Deaths from operation, and during the two months following it, total about 2 per cent. There is a considerable death-rate, amounting to about 10 per cent., from pulmonary tuberculosis, tuberculous meningitis, and intercurrent diseases after the period of two months has elapsed. Of the total deaths one half died during the first year after operation. The mortality among the younger children in operative and post-operative periods is greater than in older children.

Summary. The operation should be considered as an incident in the treatment, and fixation and mechanical support should be carried out for a period sufficiently long to afford opportunity for fusion of the bodies of the vertebrae to occur. The younger the patient, in view of the imperfect ossification of this early period, the more essential that treatment by rigid apparatus should be thorough and long-continued. A cure can hardly be considered as assured until the child has passed the second period of growth.

The Commission finds that the present methods of recording and following up cases are inadequate. J. T.

Calvé, J. Treatment of spinal caries. *J. Orthop. Surg.*, 1921, **3**, 515.

All of the author's cases are children. Three elements are necessary in treatment: first, recumbency for three years; second, hyperextension; third, open air. There are three stages in the evolution of the disease in the vertebrae: (1) infiltration, (2) destruction, and (3) repair and rebuilding of the destroyed area. The last stage never begins until the third year of the disease. In autopsies on children at Berck no repair has ever been seen before the third year. The repair is at first fibrous and afterwards bony. Bony union is always the result of juxtaposition of bony surfaces, never of the production of new bone between separated surfaces, as in fractures. Corrections of deformity produced either by treatment or by natural

processes may occur inside the focus of disease, above, or below it. Calvé analyses these corrections.

In lumbar Pott's disease. (i) Extrafocal corrections: progressive hyperextension increases the normal hyperextension of the lumbar spine. (ii) Intrafocal corrections: (*α*) Early. The upper vertebra slips backwards and downwards till the upper articular process of the lower vertebra meets the lower intervertebral notch of the upper vertebra. (*β*) Late. The laminae and pedicles which are originally less in height than the bodies, become atrophied and reduced in height. Calvé considers that there should never be any lumbar prominence after recovery.

In dorsal Pott's disease correction is much more difficult. The normal kyphosis, the respiratory movements, and the body-weight increase the deformity. Hyperextension in the dorsal region does not exist normally. The laminae and pedicles are naturally the same height as the bodies and, when deformity occurs, posterior physiological settling, as it occurs in the lumbar region, is impossible. As soon as the disk is destroyed the centre of flexion passes backwards to the articular processes. The upper vertebra crushes down on to the lower, and dislocation with separation of the laminae results. Recumbency removes the body-weight factor. (i) Intrafocal corrections are—early, none; late, slight diminution in height of the laminae and pedicles. (ii) Extrafocal corrections are necessary in order to maintain the erect posture. Natural extrafocal corrections are possible only in the cervical and lumbar regions, because only in these is hyperextension possible. The dorsal spine adjacent to the disease, which is not normally hyperextensible, helps in the production of the kyphosis.

Calvé states that in treatment the bony focus must not be opened up as, if that be done, there will be no bony union; nor is there hope for an intrafocal settling. The normal physiological hyperextension in the extensible regions must be prevented by plaster jackets. By continuous pressure above and below the focus an artificial compensatory hyperextension must be obtained, causing a remodelling of the vertebrae and disks adjacent to the focus. Gradually the vertebrae open in front, and the laminae, pedicles, spinous and articular processes become diminished in height.

It follows that time is the prime factor in the treatment. Operations for fixation are incompatible with this method of treatment. A graft would prevent the evolution of the corrective phenomena. Prolonged recumbency causes no injury to the moral or physical development of the child.

J. T.

Sinding-Larsen, M. F. En hidtil ukjendt sygdom i patella. [**A hitherto unknown disease of the patella.**] *Norsk Mag. f. Lægevidensk.*, 1921, **82**, 856–8.

Sinding-Larsen has observed two cases, the clinical and X-ray examinations of which indicated a fairly well-defined but hitherto unlabelled disease. The patients were otherwise healthy girls, aged 10 and 11 respectively, who, after overstraining themselves by dancing and jumping, complained of pain in their knees. In the first case there was a considerable but not tender swelling below and on both sides of the ligamentum patellae. There was no effusion into the joint, no thickening of its capsule, no impairment of movement. Considerable tenderness was demonstrable on percussion of the whole of the front of the patella. The quadriceps muscle

on the right side was slightly relaxed. Nothing abnormal about the left patella could be found on clinical examination. The X-rays showed the profile of the patella to be blurred on its anterior and lower aspect, and there seemed to be abnormal calcium or bone shadows in the thickened soft structures immediately in front of the patella. The space behind the patella was occupied by diffuse shadows indicative of inflammation or oedema in the fatty tissues. The outline of the left patella was clear except at its lowest point, where it was irregular. v. Pirquet's and the subcutaneous tuberculin tests were both positive, but the latter gave rise to no focal reaction in the patella. This patient wore a plaster-of-Paris splint for six weeks, and the other was simply ordered to keep quiet. After about half a year both the clinical and X-ray signs of disease had vanished. In both cases skiagrams of the apparently healthy knee revealed changes similar to, but slighter than, the changes which in the other knee had given rise to clinical symptoms. Sinding-Larsen suggests that this condition is a periostitis or epiphysitis, due to overstrain, and he observes that a similar condition has recently been described by Sven Johansson. C. L.

v. Stapelmohr, Sten. Beitrag zur Kenntnis der subkutanen Sehnenrupturen und Deckung von Sehnendefekten durch freie Sehnentransplantation. [B.] [**A contribution to the study of subcutaneous tendon ruptures and the repair of gaps in tendons by free tendon transplantation.**] *Acta Chir. Scand.*, 1921, **54**, 177–209.

v. Stapelmohr ranges over a wide field, but the chief feature of his paper is the discussion of rupture of the long extensor of the thumb in connexion with a Colles fracture. At his hospital, where about 75,000 surgical cases have been attended to in the past ten years, only two examples of this condition have been observed, and they occurred within three weeks of each other. The first patient was a tailor, aged 40, who fell from a height of 6 metres on to his right hand. A typical Colles fracture, with dorsal displacement of the lower fragment, was diagnosed, and after it had been set the X-rays showed satisfactory reposition. At this stage the movements of the thumb seemed to be unaffected. But about eight weeks later, while he was attaching a ring to his watch chain, he experienced sudden pain in the extensor aspect of the right wrist, and he found that he could no longer extend the thumb. Examination showed rupture of the long extensor, and when its sheath was opened it was found to be empty, the proximal end of the tendon having been drawn up by retraction of the muscle. As the two ends could not be united, tendon grafting was performed, and with success. In the second case there was no displacement complicating the Colles fracture; no manipulation was, therefore, required to set it, and it was thus evident that the rupture of the tendon which occurred three and a half weeks later could not be laid at the door of the surgeon who set the fracture.

v. Stapelmohr's study of the literature has yielded records of 8 cases, all of which were remarkably similar to his own. The patient's ages ranged from 26 to 60 years, and in as many as 8 of the 10 the side affected was the right. In one case as long an interval as 18 months elapsed between the original injury and the giving way of the tendon. In the remaining cases this interval varied from 4 to 10 weeks, and no relation could be established between the length of this interval and the severity of the

original lesion. The point of rupture is immediately distal to the styloid process of the radius and the dorsal ligament of the wrist, and in five out of the seven cases which were operated on the torn ends of the tendon were found to be frayed out. Another peculiarity is the apparent triviality of the movement which finally ruptures the tendon; in v. Stapelmohr's second case the patient was pushing a hat-pin into her hat when the tendon suddenly gave way to the accompaniment of severe pain. The mechanism of this injury to the tendon is probably the following: At the point where the tendon leaves the distal end of its sheath it forms a bend, and this bend is exaggerated when, as the patient puts out his hand to protect himself as he falls, his thumb is sharply abducted while his hand is extended at the wrist and radial-flexed. With the hand in this position, and the muscle of the long extensor of the thumb suddenly contracted, the tendon is forcibly stretched and kinked on its sheath at its distal end. The injury thus inflicted at this point is promoted by the inadequacy of the blood-supply in patients who have passed the age of 25, and it is followed by slow necrosis and little evidence of an inflammatory reaction. C. L.

Hernaman-Johnson, F. The Carelli method of perirenal inflation—an account of a recent demonstration. *Brit. M. J.*, 1922, ii, 91.

The author gives an account of a demonstration given at the French Hospital, London, by Dr. Carelli, of Buenos Ayres. Gaseous inflation of the abdominal cavity does not display the whole kidney to radiography, inasmuch as the organ is retroperitoneal; but Carelli showed that an injection of oxygen into the perirenal tissues made the kidney plainly visible on the fluoroscopic screen and on the photographic plate.

500 c.cm. of the gas was injected slowly through a fine platinum needle about 10 c.cm. long. The needle was inserted over the transverse process of the 2nd lumbar vertebra; the position of this structure was found (1) by tracing the last rib to its junction with the spine and taking a point 2 cm. below the angle and the same distance from the middle line (the 2 cm. is an average measurement only); and (2) by counting the spinous processes upwards from the 4th lumbar and taking a point midway between the 2nd and 1st, as giving the required level.

He pushed the needle in vertically until stopped by the bony transverse process and then altered the direction of thrust, working the point slightly outwards and forwards until it cleared the obstruction. At a depth of 6 cm. he estimated that he had reached the perirenal areolar tissue.

Having waited to see that no blood welled up in the needle, he connected with the manometer of an oxygen container similar to that used for inducing artificial pneumothorax. The manometer should show oscillations, up with inspiration, down with expiration — the reverse of the movements that would have been seen if the needle had been in the pleural cavity. If no manometer movements are seen, a few cm. of gas should be slowly introduced; then either these movements will appear and the injection become possible, or pain other than a dull ache will be caused; the latter occurrence indicates the necessity for retrial.

The author considers that the method will prove of value to clear up doubtful cases; it renders visible changes in renal size and shape and also calculi too faint to be seen in ordinary radiographs.

The risks seem to be small. Carelli has done it several hundred times without mishap.

CO_2 should be used in preference to oxygen, as it is more rapidly absorbed after the examination.

[Note by Abstractor.—Would it not be easier to introduce the needle with the help of the fluoroscopic screen ?] C. C. C.

Mandl, F. Zur Statistik der postoperativem Lungenkomplikationen und über erfolgreiche Bestrebungen zu deren Prophylaxe. [**Statistics of post-operative lung complications and successful attempts in their prophylaxis.**] *Deutsche Ztschr. f. Chir.*, 1921, **165**, 67.

The first part of this article is a discussion on the aetiology of lung complications after operations, based on statistics taken from eight different years of the last thirty. The influence of local anaesthesia has been investigated, and the author comes to the conclusion that there is no striking difference between the cases operated upon under local and those under general anaesthesia, but that the lung complications are more dependent on the site and nature of the operation than on the kind of anaesthetic used ; that operations involving the abdominal cavity, and more particularly the upper half, are those which are most frequently followed by respiratory trouble. In operations on the stomach resections were more often so complicated than were gastro-enterostomies. Operations on the neck did not present the same morbidity as abdominal operations, and the conclusion is drawn that lung complications are not so much due to aspiration as to hypostatic congestion and retention of secretion in the lungs.

The second part of the paper is an account of an attempt to reduce the frequency of lung complications, which were found to be unusually frequent in the winter 1919–20 in Vienna, due, it is supposed, to the inadequate heating arrangements in the hospital. The particular method used was an injection of digipurat, a preparation of digitalis, immediately after the operation, and it is claimed that the percentage of lung complications was reduced from 27 per cent. to 8 per cent. It is suggested that the digitalis had an influence on the pulmonary circulation. G. E. O. W.

Kummer, R. H., and **Brutsch, P.** Calculose vésicale géante, diverticulaire et libre. [**Gigantic vesical calculi, encysted and free.**] *J. d'urol. méd. et chir.*, 1921, **12**, 175.

The case quoted is that of a male, aged 64, who was admitted to the surgical clinic on September 4, 1919. He had had gonorrhoea at the age of 30. From the age of 34 he had had irritation of the bladder coming on without apparent cause. Since the age of 40 he had sometimes passed blood in the urine. From the time the haematuria started he had frequency of micturition, and the urine had been turbid from time to time. Since 1905 he had had a kind of lumbago which radiated into the legs; during these crises the urine became thicker. The frequency was worse at night and not affected by hard work; it became more constant and difficulty in micturition commenced, the stream being at times interrupted during micturition; the patient had to strain on micturition and the stream became weak. This condition got worse and the urine was alternately thick and clear; when it was thick he had a pain in the penis, and also had frequent false calls to micturate, followed by the passage of up to 2 litres.

Once or twice he had passed gravel. Since 1918 the urine was constantly purulent.

On examination the tongue was dry and dirty. Obstinate constipation, interrupted by attacks of diarrhoea, was present. The bladder dullness extended two fingers' breadth above the symphysis pubis even after catheterization. On rectal examination the prostate was firm and flattened; in the position of the right lobe a painless, globular, smooth swelling of bony hardness was felt bulging back into the rectum and extending laterally to the pelvis; bimanually, a mass of the same consistence could be felt above the pubes; pressure on the mass in the rectum caused slight movement of the abdominal mass. The calibre of the urethra was normal till the membranous urethra was reached, where a large variety of instruments was obstructed. A coudé catheter was finally passed, which drew off a small quantity of extremely purulent urine; a grating was felt on the catheter; the instrument entered the bladder a considerable distance, but felt wedged in the bladder and could not be rotated. A diagnosis of vesical calculus was confirmed by X-ray examination.

On September 17, 1919, under ether, a suprapubic cystotomy was performed and two large free calculi removed. An enormous calculus incarcerated in a sacculus was found projecting into the bladder a little to the right of the neck. This was removed by incising the vesical wall over it to the right of the middle line from behind forwards. The three calculi weighed together 585 gm., and the one in the sacculus 350 gm.

When the suprapubic fistula healed the patient could not pass a drop of urine by natural means, and his attempts to do so broke down the suprapubic fistula. This closed again on tying in a catheter, and the experiment was repeated several times with the same result. The patient was still leading a catheter life in October 1920, holding 1 to 2 litres before he had a desire to micturate. On rectal examination the prostate had a normal volume and consistence. F. J. F. B.

Sistrunk, W. E. The indications for surgical treatment in the different types of goitre. *Surg. Gynec. & Obst.*, 1921, **33**, 348.

Plummer, after studying a thousand cases, claims that there are only three types of goitre—colloid, adenomatous, and exophthalmic—and that all other types are variations or combinations of these three. Sistrunk states that the colloid goitre is definitely a change of youth, and is most frequently seen between fifteen and twenty-five. It is not infrequently associated with nervous symptoms and tachycardia, so that it may closely resemble the exophthalmic goitre. The basal metabolic rate is, however, normal or slightly lower, and this gives a certain test between the two conditions. It often produces no symptoms, and microscopically it shows acini that are dilated and filled with colloid, while the epithelium lining the acini is low and flat. It is the only type which disappears with the administration of iodine and thyroxin and should not be considered to require operation.

The adenomatous goitre is the commonest. It seemingly develops in middle age, but probably arises in early life. The enlargement is due to encapsulated adenomata which have probably developed from foetal rests. They often produce an enormous enlargement of the thyroid and are prone to degenerate, so that they may become haemorrhagic, cystic, or calcareous. Mild hypothyroidism, with a relatively low metabolic rate, may be

present. Sometimes hyperthyroidism may be present, but then the cardiovascular system usually suffers more severely in distinction to true exophthalmic goitre, where the nervous system is mainly affected. They are, in the majority of instances, best treated by surgical measures, but in younger persons it is best to defer operation until the age of twenty-five or thirty unless there is evidence of pressure.

Exophthalmic goitre may occur at any age. It is most often seen in the third and fourth decades. It may develop suddenly or insidiously, and sometimes all the symptoms of hyperthyroidism may be present without any enlargement of the thyroid. The disease is characterized by severe periods, each of which is spoken of as a thyroid crisis. The gland is symmetrically enlarged and hard. Microscopically, the epithelium is hypertrophied and there is very little colloid. The best results are obtained by surgery, but certain patients may recover with medical treatment. There is considerable danger in allowing medical treatment, as secondary changes may occur. Although the mortality following operation has gradually decreased there are still some patients who must be operated on with relatively high risk. If there have not been severe secondary changes and the metabolic rate is low, thyroidectomy may be done with comparative safety, but if toxic signs are marked a preliminary ligation of the vessels may be necessary. The reaction after ligation is less than that following thyroidectomy. Operation is always dangerous during and immediately after a crisis. The basal metabolic rate is a great aid in diagnosis and is a definite index of the amount of hyperthyroidism. A. J. W.

Halsted, W. S. The operative story of goitre. *Johns Hopkins Hosp. Bull.*, 1920, **19**, 71.

The author gives a complete review of the history of the operative treatment of goitre. He sketches briefly his own interest in the subject and states that in 1879–80, while he was working in Vienna upon the thyroid gland in the fish, he does not recall seeing a single operation for goitre in Billroth's clinic. From 1880 to 1886 he only saw one such operation in New York, when he assisted at an operation in which the patient was in the sitting posture with a rubber bag tied round his neck to collect the blood, and at the operation only two artery forceps were in use. The article is a monumental work which gives a complete review of the literature on the subject, and includes no less than 375 references.

The story of the modern technique is very largely traced by means of extracts from the various papers. The earliest account of an operation upon the thyroid is apparently that of Albucasis, which was performed somewhere about the year 330. From this time there was practically no progress with the exception of a few rather doubtful reports in the fifteenth, sixteenth, and seventeenth centuries, until the eighteenth century. It is of interest to note that in 1596 an attempt was made to remove a goitre from a ten year old girl. She died under the operation and the surgeon was imprisoned. A case reported by Gooch in 1770 was followed by severe haemorrhage, which was controlled by compression day and night for eight days by persons alternating with each other at the task.

In the first fifty years of the nineteenth century about a hundred cases are quoted, but the mortality was extremely high and the operation was strongly condemned by such surgeons as Robert Liston, J. Dieffenbach, and S. Gross. A quotation from the last of these three throws a most

interesting light upon the progress which has been made in the last sixty years, although it is too long to reproduce here. In 1869 Billroth had performed the operation twenty times with eight deaths, and it was his work especially which gave the impetus to this branch of surgery. The severity of the operations as carried out in this period, when there was no anaesthesia, when arterial forceps were not yet discovered, and when the tumour had reached an enormous size before surgery was considered, is well shown by the full account which is given of the operation performed by Dupuytren. Long and careful extracts are given of most of the reported earlier operations, and in the accounts of them all it is easy to realize how extremely dangerous and difficult the operation was. Apparently somewhere between 1877 and 1880 forceps first began to be used, with an immediate improvement in the results, which have now reached such a stage of perfection that it is indeed difficult to realize that the great danger of this operation used to be the absolutely uncontrollable haemorrhage. In 1879 a series of successful cases by Billroth were reported, and included sixteen in the antiseptic series. Of a total number in which he performed the operation in the pre-antiseptic era thirteen died out of thirty-six, whereas in the antiseptic period there were only four deaths in forty-eight cases.

Kocher's work commenced in 1874, and he was the first to realize the fact that complete removal of the thyroid was followed by the disastrous results which are so clearly recognized to-day. His papers, which are fully reviewed by Halsted, show the enormous progress which has been made, especially in the treatment of exophthalmic goitre, and in 1895 Kocher was able to review his first thousand cases of operations for goitre. Halsted then reviews the progress of his own work in America, and gives an account of his own operation which is now so well known. This portion of the work is the most brief of the whole, and from it one would hardly appreciate that Professor Halsted has practically lived through the whole period of modern progress in these operations, and has indeed done so much to produce the successful modern results. Although so brief an abstract is alone possible, the article is the most complete which has yet been published. A full account of the progress of this branch of surgery is given with very complete abstracts of every paper of note. A. J. W.

Sistrunk, W. E. The surgical removal of pancreatic stones. *Ann. Surg.*, 1921, **74**, 380.

Pancreatic stones are rare, and very few cases have been reported in the literature in which a pancreolithotomy has been performed. It is probable that they are often overlooked at operation, although multiple calculi may give rise to a feeling of crepitation. Single stones may be more difficult to recognize, owing to the consistency of the gland. Although at the Mayo Institute the pancreas is examined in every operation upon the upper abdomen, there have been only four operations for removal of calculi during eleven years.

The calculi closely resemble those found in the salivary glands. They are usually white or slightly grey in colour, fairly firm and irregular in shape. They may occasionally be faceted. It is probable that their formation is dependent upon infection of the ducts or stagnation of the pancreatic fluid from obstruction. Diabetes has often been observed with stones. In Hansemann's seventy-two cases of diabetes associated with pancreatic

disturbances, stones were present in twelve, and in Oser's seventy cases of calculi diabetes was recorded twenty-four times. They have been reported in association with cysts, of which they may be the cause.

The symptoms are very similar to those of chronic pancreatitis associated with gall-stones, so that a definite diagnosis can be made only at operation, hence the pancreas should be carefully palpated in every operation carried out for infection or calculi in the bile-passages. The calculi may be single or multiple, or may entirely fill both the pancreatic ducts. They have also been found near the periphery of the gland, where they are formed in the small ducts. In one case a ridge could be felt throughout the whole course of the pancreas, due to a dilated duct. Operations for removal of the calculi present no unusual difficulties. The gland should be exposed either through the gastro-colic or the gastro-hepatic omentum, according to whether the stomach is high or low. Cases have been reported in which the stone has been removed by opening the duodenum and slitting up the papilla of Vater. If the ducts are opened, free drainage should be supplied down to the wound after the ducts are closed.

Four cases are reported at length. In the first case a stone the size of a filbert and several smaller ones were removed through an incision in the anterior wall of the duodenum. In the second the duct was felt dilated, and many stones were removed through a free incision made into it. In the third case many stones could be palpated in the head of the pancreas; they were removed through an opening made in the mesentery of the duodenum. In the fourth case a similar approach was used, and two stones the size of navy beans were removed. A. J. W.

Archibald, E., and **Gibbons, E. C. Further data concerning the experimental production of pancreatitis.** *Ann. Surg.*, 1921, **74**, 426.

There are three theories as to the cause of pancreatitis: (1) that bile enters the pancreatic duct owing to obstruction of the common duct from a stone, a shred of mucus, or a spasm of the sphincter; (2) that an infection travels from the gall-bladder along the lymphatics to the head of the pancreas; (3) that the duodenal contents are forced into the common duct through the papilla, and so into the pancreatic duct. The first and third may be considered as proved for a considerable proportion of the acute cases. The second is still under discussion. There appears to be no doubt that the first method is by far the most common. The authors show that, in cats, fluids such as water, bile, and a solution of bile salts may be run from the gall-bladder under the pressure of from 300 to 600 mm. of water into the pancreas, and that even the finer radicles between the acini will be found filled with the solution. In such cases the only possible obstruction is the resistance of the common duct sphincter. They say that three conditions may probably be present: (1) an increase in the amount of bile salts in the bile; (2) undue resistance of the common duct sphincter; (3) abnormal rise of pressure in the biliary system behind. Spasm of the sphincter may be due to hyperacidity of the duodenal contents, as is suggested by three cases published by W. J. Mayo, in which pancreatitis was found in association with duodenal ulcer. The increase in the amount of salts in the bile is probably brought about by the effect of gall-stones, especially if associated with inflammation.

They have been able to produce all grades of pancreatic necrosis by

injecting ox bile and human bile from an acutely inflamed gall-bladder into the gall-bladder of cats under pressure. Their investigation as to the effect of infection upon the concentration of bile salts has not yet produced any definite result, but it was noticeable that the injection of infected bile led to a much more extensive necrosis than did non-infected bile.

They believe that the abnormal rise in pressure in the biliary system is due to the forcible contraction of the gall-bladder, and that cholecystectomy sometimes cures a co-incident pancreatitis, partly because it diminishes the pressure and also removes the source of infection. A. J. W.

Ochsner, A. J. Drainage of abscess of the pancreas. *Ann. Surg.*, 1921, **74**, 434.

The author reports a case of a woman, aged 48, who was operated upon for an ulcer of the stomach which had become carcinomatous. At operation an indurated mass was found attached to the tail of the pancreas, and was evidently an abscess which had formed in the tail owing to an infection which had originated in the perforation of a gastric ulcer. The position of the abscess was determined through the anterior incision and a second incision then made in the left flank, immediately below the last rib, and a pair of forceps passed forward. The opening was deepened to a point immediately behind the pancreas. The abdominal wound was closed and the posterior wound loosely packed with gauze. Five days later the abscess burst spontaneously and drained through the posterior wound.

A. J. W.

Delatour, H. B. Traumatic pancreatitis. *Ann. Surg.*, 1921, **74**, 435.

Traumatic lesions of the pancreas are very rare. Stuart, in 1921, collected fifty-four cases, including one of his own, but this did not include involvement of the pancreas in perforating wounds. The case reported by Delatour was the first occurring in two hospitals in thirty years. The author states that Wallace could only find five cases of injury of the pancreas in 965 penetrating abdominal wounds.

The case reported is one of a boy, aged 13, who was knocked down by a wagon, the wheel of which passed diagonally across the abdomen. On admission there was no abdominal distension, and only symptoms of slight shock. In the first twelve hours he complained at intervals of severe pain and vomited bile-stained fluid frequently. Next morning there was some rigidity of the recti and tenderness in the epigastrium. An operation was therefore performed, when a considerable quantity of blood-stained fluid and clots were discovered in the peritoneum. The head and about half of the remainder of the pancreas was found lacerated and contused. The pancreas was exposed and drains were led down to it. During exploration extensive areas of fat necrosis were observed. After the operation considerable shock was experienced. For the next two months he continued to have irregular attacks of pyrexia with some discomfort and abdominal distension. A mass rapidly formed in the upper abdomen and a second operation was performed, an incision being made in the back just below the twelfth rib, two inches to the right of the spine. Through this incision a mass was found just internal to the upper pole of the kidney. This was incised and three pints of clear fluid escaped. A drainage-tube was inserted. After this he rapidly

improved. He has been frequently seen since and there has been no recurrence of his symptoms.

Delatour lays stress upon the value of the posterior incision as being the simplest and most direct route of reaching and draining cysts or abscesses of the pancreas. A. J. W.

NEUROLOGY

Golla, F. The objective study of neurosis. The Croonian Lectures, Royal College of Physicians, London, 1921. *Lancet*, 1921, ii, 115, 215, 265, 373.

There is no aspect of neurology which has been more discussed and disputed, or which has been the excuse for such a locust plague of books within the past few years, as that comprehended by the neuroses and psychoneuroses. This is not an opportune moment to discuss the merits of much of what has been said and written on the subject, but it may be remarked with some reason that not a little of it has been unnecessary and wearisome reiteration, of no more value than to indicate the unquenchable apostolic zeal of its devotees. Into the stale and heated atmosphere thus engendered, these lectures come as a welcome breath of fresh and independent thought. Golla has applied to the study of neurosis the physiological method advocated by Pawlow, and used by him with such brilliant results in the production and investigation of 'conditioned reflexes'. In reading Golla's methodical study of the psychogalvanic reflex, one cannot help contrasting it with some recent writings on this subject by clinical psychologists, which savour more of the musings of some mediaeval alchemist than a scientific statement of a physical phenomenon. Admittedly the phenomenon is a reflex reaction, and it is therefore capable of precise description. The nature of the adequate stimulus, the time relations of the response and the various factors which modify it, its facilitation and inhibition, should all be capable of definition. For the first time, as far as we are aware, a thorough investigation on these lines has been carried out for the psychogalvanic reflex. Golla shows clearly that it belongs to the class of what Sherrington has called 'nociceptive reflexes', that is, reflexes which result from the application of stimuli of nocuous character, which threaten the well-being of the organism in some way. The psychogalvanic reflex is no longer a conjuring trick in the hands of the psychotherapeutic mystagogue, but a physiological reaction comprehensible to the plain man.

The object of the simple and fascinating experiments described by Golla has been to analyse the specific and general bodily reactions which accompany the processes of thought and feeling, with a view ultimately to determine the mechanism of production of the neuroses. The lectures are too concise for us to detail these experiments, but they include the study of the tonic muscular reaction to mental effort, the psychogalvanic response and its relation to affective states, and other objective bodily reactions to nocuous stimuli, both mental and physical. In considering the relation of an affective state to the bodily reaction associated with it, he finds that the stimulus is perceived, differentiated, and acted upon before the sensory concomitant of the bodily reaction can be experienced as an

affective state. This is an interesting commentary upon the James-Lange theory of emotion, which has been so hotly contested by psychologists who have never troubled to put the matter to experimental proof. The author's discussion of instinct and instinct reflexes is a refreshing variation upon much of the imaginative psychological lore which has recently accumulated round the subject. In his final lecture, Golla indicates the bearing of his observations upon the genesis and treatment of the neuroses. We wish he had given us more than this attractive glimpse into a field in which it may be hoped he is continuing to work. In any case, we cannot be too grateful to him for this charmingly recorded attempt to rescue the subject from the wordy morass into which it has been plunged of late years.

F. M. R. W.

Tilney, F. The functional significance and principal syndrome of the cerebellum. *Neurol. Bull.*, 1919, **2**, 289.

Sherrington, C. S. (1). ***The integrative action of the nervous system.*** Constable, London, 1906.

Sherrington, C. S. (2). **On plastic tonus and proprioceptive reflexes.** *Quart. J. Exper. Physiol.*, 1909, **2**, 109.

Sherrington, C. S. (3). **Reflex inhibition as a factor in the co-ordination of movements and postures.** *Quart. J. Exper. Physiol.*, 1913, **6**, 251.

Sherrington, C. S. (4). **Postural activity of muscle and nerve.** *Brain*, 1915, **38**, 191.

Tilney's paper is divided into three parts: (i) a general view of the significance of the cerebellum, (ii) its functions, and (iii) the principal cerebellar syndrome. In part one, the author briefly reviews the evolution and phylogenetic history of the organ as follows: It is a supra-segmental structure, developed upon, and not as a part of, the segmental nervous system. Like the other supra-segmental parts of, the nervous system, the cerebral hemispheres, and the tectum of the midbrain, its grey matter is superficial and its white matter central. It is an organ of great antiquity, being found in certain invertebrate forms. Its development throughout the animal kingdom is in direct relation to the range of motor capacity of the particular animal type in question. Therefore it is greatest in man, who, in addition to the primitive locomotor functions of the lower limbs, has developed a highly complex motor activity in the upper limbs. Throughout the animal kingdom its internal structure is strikingly uniform. Its morphology, as elucidated by Elliott Smith and by Bolk is briefly stated, and its fibre connexions tabulated.

This chapter concludes with some highly speculative conclusions by the author. In part two, the history of physiological research on the cerebellum is somewhat sketchily reviewed, and the clinical evidence as to topographical representation of the different regions of the body musculature in the cerebellum is given somewhat more fully. Synthesizing all these observations, Tilney concludes that the cerebellum is essential to motor co-ordination, quoting Babinski to the following effect: 'Every form of active muscular exertion necessitates the simultaneous co-operation of immense assemblies of synergic movements throughout the body to secure steadiness and maintain general equilibrium . . . the cerebellum is the centre of these unconscious adjustments. . . .' Mills and Weisenberg, dissatisfied

with Luciani's analysis (*Medical Science*, 1921, **5**, 136), have interpreted the cerebellar syndrome to indicate that synergia is the fundamental function of the cerebellum and asynergia its essential defect symptom. The other symptoms described are particular manifestations of this, while atonia is a secondary effect. Synergia is taken to mean the faculty of combination of the various components of a complex act. The various manifestations of asynergia are then described in detail.

From this point Tilney develops his own theory of cerebellar functions. As a result of cinematographic recording and subsequent analysis of the disorders of movement in cerebellar cases, Lambert and Tilney conclude that synergia is dependent upon two factors: first, the establishment and maintenance of 'synergic units' throughout the body; and second, the establishment and maintenance of co-ordination between the synergic units in the performance of complex acts.

Throughout the body the muscles are supposed to be arranged in unit groups, each consisting of agonist and antagonist. But these do not act antagonistically, as is taught. They are antagonistic in the anatomical sense alone. Physiologically they are synergists, both contracting simultaneously, though not equally. The more powerfully acting muscle, the agonist, is called the 'dominant element', and the other member of the pair, which contracts less powerfully, the 'check element'. Normally, the activities of each is co-ordinated, but in asynergia, the proper co-operation of the two is lost. The check element is too feeble, the range of movement is excessive, and correction follows. This in turn is excessive, and so movement takes on a jerky oscillating character. In complex movements this process is repeated throughout the body musculature. 'Simple synergia' is the normal co-ordination within the synergic unit. 'Integrative synergia' is the perfect co-ordination of different synergic units. In every motor act there is a 'kinetic' and an 'akinetic' phase, by which the authors may be taken to mean movement and the maintenance of any position reached, and these two phases must also be perfectly co-ordinated in perfect integrative synergia. Therefore, when co-ordination within the simple synergic unit is lost, integrative synergia is in turn disordered and the characteristic asynergia of cerebellar lesions results. Tilney believes that there is a definite topographical representation of the different synergic units in the musculature in the cerebellar cortex. Part three consists in the detailed account of a case of cerebellar disease in the light of these conclusions.

The reader acquainted with recent physiological work on the nervous processes concerned in the co-ordination of movement will find Tilney's hypothesis of some interest. At the same time he cannot but remark how much farther the author might have gone but for the self-denying ordinance by which he has apparently declined to avail himself of the wealth of exact knowledge on the nervous mechanism of co-ordination provided by the researches of Sherrington. These have already carried us far beyond the simple conception formulated by Tilney. It must be remembered that in attempting to analyse disorders of movement into their ultimate components the clinical observer labours under great difficulties. He cannot see the various muscular contractions, postures, and relaxations which go to make up a movement. All that he can hope to see is the resulting movement, the algebraical sum of many synergic and antagonistic reactions, all of which are completely hidden from him. He is, therefore, commonly reduced to evolving his theories of co-ordination and his explanations

of the different forms of inco-ordination largely from his inner consciousness, with what results the numerous and conflicting analyses of cerebellar ataxy and of the extra-pyramidal symptom complex only too clearly show. However, the many experimental observations of Sherrington on the nervous processes underlying co-ordinated movement have placed in our hands a weapon of incalculable value in the interpretation of the disorders of movement observed in man under the conditions of disease. From this source we have learned that there are two components in movement, phasic and tonic or postural. Each has its central nervous mechanisms laid down in the segmental nervous system, and all these are at the service of the cerebral motor cortex for the production of the voluntary movements of the organism. In the control and elaboration of postural reactions there is reason to suppose that the highest cerebral motor centres act upon the segmental nervous centres employed in tonic or postural reactions through the medium of the cerebellum. Muscle-tone is the basis of all postural reactions, and when this is lost all postural reactions are abolished. Now posture is as essential an element of co-ordinated movement as the actual movement of the limbs through space. Therefore, when tone is abolished, gross disorders of co-ordination must result. If we study the results of atonia as they are to be seen in the reflex reactions of the experimental animal, we find that *they include each and all of the defects of co-ordination which make up the cerebellar symptom-complex.* It is clear, then, that any attempt to determine the nature of cerebellar ataxy and that of normal co-ordination of movement demands as an essential preliminary a thorough acquaintance with the physiology of muscle-tone, its maintenance, regulation, and purpose. At the head of this review we have placed a list of references to the papers in which Sherrington has recorded his classic observations on these subjects. We cannot conceive how the neurologist can hope to formulate theories of co-ordination and of inco-ordination without this fundamental information. F. M. R. W.

Hall, H. C. *La dégénérescence hépato-lenticulaire (Maladie de Wilson : Pseudo-sclérose).* [***Hepato-lenticular degeneration.***] Masson et Cie, Paris, 1921.

Since the publication, in 1912, of Kinnier Wilson's classic paper on progressive lenticular degeneration, an ever-increasing interest has been taken in that strange group of cases presenting one or other variety of 'extra-pyramidal syndrome' and associated with hepatic cirrhosis. As is inevitable in the delimitation of a new clinical conception, the clinical picture described by Wilson and the underlying nervous lesion have proved to be somewhat too sharply defined in the light of the more recently observed cases. When writing his paper Wilson was able to find but eight similar cases in the literature, but now no less than sixty-eight cases have been recorded. A more catholic interpretation of the clinical and pathological pictures has allowed the identification of some of these from the literature of as far back as 1883, but most of them, and certainly all the adequately described instances, have been recorded since 1912.

Not only did Wilson thus draw attention to and elaborate a new clinical entity, but his observations have also brought to notice the whole question of what are called 'extra-pyramidal motor diseases' and that of their value as indicating the probable functions of the corpus striatum. In

the present book, the Danish neurologist, Hall, has summarized all the clinical observations up to date and has added several cases which have come under his own personal observation, and he has presented his readers with an admirable summary of such knowledge as we possess of the subject, in its clinical, pathological, physiological, and aetiological aspects. A preface by Professor Pierre Marie, to which we shall refer later, is a valuable addition.

Wilson described, under the title of 'progressive lenticular degeneration a familial nervous disease associated with cirrhosis of the liver', four personally observed cases of a condition characterized by a series of motor disorders of function, muscular rigidity, tremor, difficulty in articulation and deglutition, and also by terminal symptoms of dementia. There was no true paralysis, no sensory changes, and no pathological alteration of the reflexes—in a word, there was no sign of interference with the functions of the pyramidal system.

Autopsy revealed the presence of bilateral and strictly delimited degeneration and necrosis of the lenticular nuclei, and of no other lesion in the nervous system; and even more striking and unexpected was the constant presence of well-marked cirrhosis of the liver, a condition which had given rise to no symptoms during the lives of the patients.

He regarded the nervous lesion as systemic, and upon the clinical picture developed an hypothesis of the functions of the corpus striatum, with the details of which we cannot now deal.

Ever since 1883, when Westphal described the earliest case, German neurologists have from time to time recorded rare cases of a nervous disease presenting symptoms suggestive of disseminated sclerosis, without discoverable lesion in the nervous system, and frequently associated with cirrhosis of the liver and with a peculiar pigmentation of the periphery of the cornea. Most of the clinical and pathological records were extremely incomplete, and it has been only since the appearance of Wilson's paper that precision has crept into the accounts of fresh cases, and as a result it is now generally held that this disease, which Westphal and Strümpell named 'pseudosclerosis', is but a clinical variation of progressive lenticular degeneration. The chief difference is simply one of the relative intensity of the different symptoms which make up the complete symptom-complex. In 'pseudosclerosis' tremor or other forms of involuntary movement have predominated, while the rigidity and fixed attitudes so characteristic of Wilson's cases, have been minimal. Further, psychical disturbances were not noted, nor in some instances any disturbance of speech.

But, as Hall clearly shows, there is no essential difference, and there are now on record cases presenting every grade of transition between the sharply defined clinical picture of Wilson's disease and the vaguer conception included under the diagnosis of pseudosclerosis.

The essential elements of the clinical picture are disturbances of muscle-tone, the nature of which are by no means understood, the presence of involuntary movements, which may be of the tremor variety, athetoid, choreiform, or of the more extensive form known as 'torsion spasm' (*Medical Science*, 1920, **2**, 67). The patient's voluntary movements are slow, and the subject tends to be fixed in persisting attitudes without permanent contracture. There is no true paralysis and no signs of any interference of function in the pyramidal system. Sensory changes are absent. Generally, there tends to be a gradual dementia as the disease develops. In many

cases, of both types, a peripheral zone of brownish-green pigmentation has been observed in the cornea.

Post mortem there are found profound cirrhotic changes in the liver, which is shrunken. The spleen is frequently enlarged, and the posterior layer of the cornea round the limbus is the seat of thickly-scattered fine pigment granules. On section of the brain, there may be gross macroscopic changes in the lenticular nuclei, necrosis, and cyst formation, or there may be minimal or no change observable. Microscopic examination reveals extensive degeneration and destruction of the lenticular nucleus, involving nerve-cells, with proliferation of glia-cells and the appearance of abnormal forms of glia-cell. The vessels are proliferated but otherwise normal, and there are no inflammatory phenomena. There is degeneration of the efferent fibres of the lenticular nucleus in the ansa lenticularis. In Wilson's cases no other lesion was found, but in the more recently studied cases it has been found that there are also nerve-cell degeneration and glial nuclei proliferation diffusely scattered throughout the cerebral hemispheres, in the basal ganglia, red nucleus, and dentate nucleus. In other words, the disease is not, as was once supposed, a pure system disease.

In the circumstances it is becoming increasingly clear that we must be very cautious in any inferences we may draw as to the functions of the corpus striatum from such material, and it is questionable whether we have any right to describe the clinical picture as a syndrome of the corpus striatum. We have already seen in *Medical Science* (1920–21, **3**, 353) to what a high degree of elaboration such speculations have gone.

In this connexion, Professor Pierre Marie in his preface expresses his scepticism as to the physiological value of the cases. He observes that he has examined hundreds of brains in which the lenticular nuclei have been involved in the 'état lacunaire', which he has described, but in which the so-called syndrome of the corpus striatum has been conspicuously absent.

Hall describes the disease, for which he proposes the name hepatolenticular degeneration, from every aspect, and thus provides in a concise form an account which is as interesting as it is valuable.

F. M. R. W.

Brüning, F., und **Gohrbandt, E.** Ein experimenteller Beitrag zur Pathogenese der Schmerzen bei der Darmkolik. [**An experimental contribution on the pathogenesis of pain in intestinal colic.**] *Berl. klin. Wchnschr.*, 1921, **58**, 1431.

The authors preface their observations with a quotation from an earlier paper by one of them (Brüning) to the effect that, whereas previous students of the problem of gut sensibility claim to have employed adequate stimuli in their work, yet in fact they have not done so, since the serous coat alone has been stimulated. The adequate stimulus must reach the mucous surface, that is, the stimulating object must be within the lumen of the gut. However, they are mistaken in supposing that this physiological point is unknown, as a perusal of the literature of other countries would have taught them. The term 'adequate stimulus' has been employed by Sherrington in discussing this particular problem (cf. *Integrative Action of the Nervous System*, p. 12). Therefore, although, as they remark, no satisfactory conclusions as to the sensory endowment of the gut have ever been reached, yet in this country, at least, the essential elements of the problem

have long ago been recognized by Head, Sherrington, and others. Nevertheless, the observations recorded in this paper are of considerable interest as a contribution to our knowledge of the problem. The authors employed dogs, cats, and rabbits for their experiments, and, to avoid the complicating effects of local anaesthesia of the body-wall at the time of making observations, they had recourse to a modification of the procedure devised by Kappis. In a preliminary operation a triangular area of the abdominal wall below the umbilicus is rendered anaesthetic by section of its nerves through two incisions which start from the umbilicus and run downwards and outwards towards the superior iliac spines. Later, the body-wall is opened without any anaesthetic and the gut exposed.

A coil of small intestine is exposed and the mucosa stimulated, either by injecting into its lumen through a fine cannula from 5 to 10 c.cm. of an irritating solution (hydrochloric acid, ether, alcohol, turpentine oil, or barium chloride solution), or by making a free incision into the gut opposite the mesenteric attachment and pouring the solution on the exposed mucosa. In this way a large area of mucosa is stimulated and the presence or absence of pain is determined by watching the animal's reaction. They find that the animal shows signs of feeling pain only when the gut goes into contraction. As soon as muscular spasm develops, and until it dies away, there is clear evidence of pain, and unless this motor reflex response occurs there is never pain. They conclude that this pain arises in the gut-wall itself, and is not a result of any pulling on the mesentery resulting from the local gut movement. Such movement is not constant, and when it occurs it is minimal and not comparable with the movement which must be of constant occurrence under normal conditions.

Further, if the mesentery be rendered insensitive by application of cocaine, the pain still develops as soon as the gut-wall goes into spasm. It has been stated by earlier observers that the application of irritative chemical substances to tissues endowed with sensibility produces a localized hyperaemia ('primäre Reizhyperämie'). This hyperaemia is constant in the mucosa of the gut, while, as Breslauer-Schück described, the visceral peritoneum, unlike the parietal peritoneum, does not react in this way. Therefore, the mucosa of the gut, and not the serous coat, is supplied with sensory nerves. They explain the apparent insensibility of the gut to surgical procedures as due to the inadequate and transient character of the stimuli applied and to the fact that the localization of the pain is not recognized by the subject.

Therefore they conclude that stimuli applied to the gut-wall elicits pain only when powerful contraction of the musculature of the gut occurs. The pain elicited is in the gut itself, which possesses sensibility.

F. M. R. W.

Wilson, J. T. The double innervation of striated muscle. *Brain*, 1921, **44**, 234.

In this paper Wilson summarizes the various morphological studies on the innervation of striated muscle. He discusses the subject under two headings, plurisegmental innervation, and innervation through the 'accessory system' of motor fibres, alleged to be of sympathetic origin.

Plurisegmental innervation. Single muscle-fibres are commonly supplied by motor fibres from more than one segmental nerve. The muscle-

fibres themselves may be plurisegmental in origin. In the case of adjoining body segments, the mesoblastic syncytium of the embryo forms a continuum connecting adjacent myotomes across intervening myosepta. Myofibrillar differentiation then occurs, so that each of the resulting muscle-fibres is polymeric. Agduhr has made some experimental observations on the force of contraction obtained from separate and conjoint stimulation of two segmental sources of nerve supply to a single muscle, and he concluded that there is an overlapping of the innervation region of separate nerves within the muscle. He also found that the region of the muscle, thus doubly innervated by adjacent segmental nerves, is greater than that doubly innervated by the peripheral nerves. This appears to indicate that a large number of individual muscle-fibres possess a double segmental innervation. Of the several end-plates which a single muscle-fibre may possess each belongs to a different segmental nerve. On the other hand, the observations of Floresco and Cavalié indicate that a single motor nerve may give off fibres to several end-plates in a muscle-fibre.

The accessory system. A second type of motor innervation of striated muscle has also been described, consisting of non-myelinated fibres which may pass to the ordinary motor end-plates which we have considered, but more commonly end independently. It has been suggested that these fibres are sympathetic in origin. It is certainly clear that they are distinct in origin from the general motor nerve supply of the muscle. Wilson points out that the conception of an accessory, sympathetic source of motor nerve supply to striated muscle is not novel, and briefly reviews the literature on the subject between the years 1882 and 1909.

Recent advances in histological technique have opened up fresh possibilities in the study of these nerve endings, and it is to the work of Boeke that we chiefly owe our new conceptions on the subject, for it has definitely established the dual innervation of muscle-fibre. Working on the development of motor nerve endings in invertebrates, he recognized a system of fine non-myelinated fibres, independent of the ordinary myelinated fibres, and ending in characteristic end-organs, in the form of fine loops or networks embedded in the sarcoplasm of the ordinary motor end-plates, and also in distinct end-plates by themselves. He was impressed by their hypolemmal position in the muscle and concluded that they must be sympathetic in origin.

With regard to the function of this system, Boeke refers to the work of Pekelharing and van Hoogenhuyze, Mosso and de Boer. The last-named claims to have proved, in the case of the frog, that the tonic innervation of muscle is carried out through these fibres and by the sympathetic system (*Medical Science,* 1921, **2**, 434). Dusser de Barenne was not able fully to confirm this observation, and Kuno definitely failed to do so, and the thesis remains unproven. However, morphological evidence is in favour of the sympathetic origin of the non-myelinated fibres in question. Wilson points out that most of Boeke's observations, in which he has attempted to differentiate the two groups of non-myelinated fibres by taking advantage of their different degeneration times, are open to the objection that his clearest demonstration of non-medullated fibres was obtained from material in which most of these fibres had been severed from their trophic centres and were already degenerating. Now a very thin myelin sheath, under these conditions, would have already suffered and might escape detection. The evidence that there are two separate systems of non-myelinated fibres

supplying the eye-muscles Wilson considers open to grave objection, and in their later paper Dusser de Barenne and Boeke appear to have abandoned the contention.

In conclusion, Wilson finds that the non-myelinated fibres are sympathetic in origin and hypolemmal in termination. Their relationships would appear to indicate that they conduct centrifugally, presumably motor impulses, which may possibly be of tonic contractile character.

A. E. B. H.

Adrian, E. D., and **Owen, R. D. The electric response of denervated muscle.** *J. Physiol.*, 1921, **55**, 326.

Henriques and Lindhard in a recent paper have argued that the electric change which occurs in a muscle on stimulation is due to a change of potential in the motor end-plate, there being no propagated electric change in the muscle-fibre itself. According to these authors, contraction of the frog's gastrocnemius in response to direct stimulation gives rise to no electric variation. Adrian and Owen have tested this hypothesis on the frog's sartorius. The sciatic nerve was cut high in the thigh and the animal subsequently pithed at varying intervals in different observations. The sartorius was stimulated at the pelvic end before and after destroying the tibial end with a hot wire. The electric response was led off by electrodes on the tibial end. After each experiment the muscles were treated with methylene blue. When an interval of thirty-six days had intervened between section of the nerve and the final experiment no trace of nerve-endings could be found in the muscle; nevertheless, in every instance, there was an electric response of diphasic character as in normal muscle. They conclude, therefore, that the nerve-endings contribute nothing to the electric response, and that the absence of response described by Henriques and Lindhard occurs only when the leads are taken from inactive muscle.

A. E. B. H.

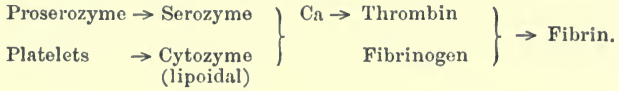
PATHOLOGY

Gratia, A. Recherches sur le mécanisme des actions anticoagulantes. [**Researches on the mechanism of anticoagulating actions.**] *Ann. d. l'Inst. Pasteur*, 1921, **35**, 513.

Under the general term antithrombin is here included a number of anticoagulant substances which all have the property of neutralizing thrombin, more or less quantitatively. The two principal types of this substance are hirudin and the antithrombin of peptone plasma. Three of the most modern theories of the coagulation of blood are critically examined by the author. It may be of interest briefly to summarize the main points of each of these rival theories.

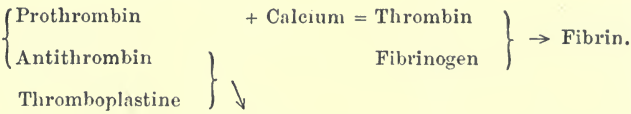
I. **Theory of Bordet and Delange.** According to these investigators the substance cytozyme is a lipoid which exists in all cells, but more especially in the platelets. Serozyme is found in the circulating plasma in an inactive state known as proserozyme. It is only at the moment of

coagulation that it appears as serozyme, and it remains in excess in the serum after the coagulation. In order that blood may coagulate, it must come into contact with foreign bodies, and then cytozyme and serozyme appear. These latter react in the presence of calcium salts to produce thrombin, which then coagulates the fibrinogen.



Thus it is rather a completion of the classical theory as contributed by Schmidt and his pupils, by Fuld and Spiro, and later by Morawitz.

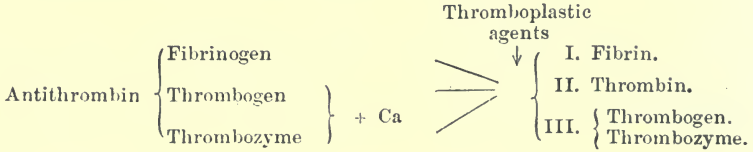
II. **Howell's theory.** Serozyme or prothrombin, as he calls it, is directly converted into thrombin by calcium salts. But this change is prevented in the circulating plasma by an antagonistic substance, antithrombin. Cytozyme he calls thromboplastine. It exists in the tissues and in the platelets, and its only purpose is to neutralize the antithrombin of issuing blood, and so to allow of the production of thrombin without entering into its composition.



Bordet has shown that this theory is incompatible with certain facts, and from the start raises a series of objections to the principles involved. The author considers it simple in appearance, but it is only adapted to the facts with difficulty, and involves many complications.

III. **Nolf's theory.** According to this author there exists in plasma three equipotential colloids, fibrinogen, thrombogen (serozyme), and thrombozyme (cytozyme). These are kept in equilibrium by antagonistic influences (antithrombin). If, however, this is broken by thromboplastic agents (such as foreign bodies, colloidal precipitates, tissue juices, lipoids, microbes, distilled water, &c.), the three colloids mutually combine in variable proportions to produce a series of complexes, more or less saturated with fibrinogen.

The complex of thrombogen and thrombozyme, rich in fibrinogen, is fibrin. That of the above two minus fibrinogen is thrombin. There remain thrombogen and thrombozyme uncombined.



This theory is based on the original and revolutionary ideas of Wooldridge. Gratia considers it too speculative in nature.

The results of the author's researches are summed up in the following paragraphs:

(1) If antithrombin prevents the coagulation of blood, it is not by the

neutralization of the thrombin, but by paralysis of its production. In a similar way it is explained why peptone plasma and hirudin plasma do not contain thrombin.

(2) The reciprocal neutralization of thrombin and antithrombin forms complexes which are stable, but heated to 60° C. they are separated and antithrombin is freed. On the other hand, the thrombin-antithrombin combination lends itself to different observations more comparable to that of the union of antigen with antibody. When thrombin and antithrombin unite in the presence of fibrinogen, for which thrombin has an equal affinity, a division of this affinity is produced. The thrombin coagulates a greater or lesser amount of fibrinogen when it has not yet completely neutralized antithrombin. In other words, it seems that the action of antithrombin on fibrinogen is opposed to that of thrombin because, owing to its affinity for thrombin, it tends to substitute itself for fibrinogen.

(3) There are great differences between the properties of peptone plasma and hirudin plasma. Whilst the first is coagulated by the addition of thromboplastic agents, such as acids, distilled water, a current of CO_2, &c., the second is quite indifferent to their action. Certain authors (Dastre and Floresco, Mellanby) even deny the existence of antithrombin in peptone plasma, for they consider it simply as an excess of alkali diverted by the liver into the circulation at the time of the peptone shock. The author has not been able to confirm this opinion. Even by using the very delicate colorimetric method of MacMariott he has been unable to detect the slightest difference in the alkalinity of peptone plasma and of normal plasma.

(4) Lipoids can coagulate peptone and hirudin plasma. This fact, which was first observed by Wooldridge, is explained in totally different ways according to which general theory of coagulation is adopted. The author's researches on this point have led him to confirm the opinion of Bordet and Delange. According to these latter, the lipoids (cytozyme) unite, in the presence of calcium, with serozyme to produce thrombin, and even enter into the composition of this agent. The author cannot accept Nolf's view. According to the latter, lipoids would be the simple thromboplastic agents, and would cause peptone plasma to coagulate just as distilled water, CO_2, and colloidal precipitates do. The similarity of the effects shown by lipoids and thromboplastic agents is only the illusion of a similarity of action. This is recalled by the fact that if lipoids are added to a serum rich in serozyme it produces, quite as well as leucocytes, platelets, or tissue juice, a large amount of thrombin, which no thromboplastic agent can do. The author has also been able to show that thromboplastic agents can only act *pro rata* with the strength of the plasma in cytozymic lipoids. Howell's opinion cannot be accepted. According to him the lipoids neutralize antithrombin, by a so-called chemical affinity which exists between them. The author has not noted any neutralization or even a weakening of the antithrombin by lipoids only, although the combined action of lipoids and serozyme will do so. That which confirms him in his opinion, is that the lipoidal cytozyme, by satisfying its affinity for serozyme, succeeds over the resistance of the antithrombin. Certain other special facts have been noted during the course of this research.

(5) The antithrombin of peptone plasma is partly adsorbed by large amounts of calcium phosphate.

(6) It is greatly weakened by a current of CO_2, but the latter does not

alter the antithrombin, since it recovers its activity if the CO_2 is displaced by a current of air.

(7) Thrombin obtained by maceration of fibrin in a hypertonic saline solution is not pure, for it contains cytozyme.

(8) Thrombin can act in a decalcified medium, but it loses at least as much of its activity as when it is oxalated. W. A. M. S.

Vines, H. W. C. The coagulation of the blood. *J. Physiol.*, 1921, **55**, 287.

In a previous paper (*J. Physiol.*, 1921, **55**, 86) it was shown that the calcium of the blood is normally present in two forms, ionized and non-ionized or combined, and that it is the combined calcium which is essential for the inauguration of normal blood-clotting. The term 'clotting complex' was applied to the combination of calcium with an undefined organic material. The present paper is an account of an investigation indicating the organic substance to which the calcium is attached, and of an attempt to prepare artificially a compound with coagulating powers, and general properties resembling those of thrombokinase. Hirudin and cobra venom seem to act primarily as antikinase. It is stated that hirudin also acts as an antithrombin. Experiments designed to test this statement show that hirudin has an inhibitory action on thrombin, whereas venom has practically none. These results are in accordance with the work of Mellanby. Thus hirudin appears to act on that factor of the clotting mechanism which is in greater concentration, kinase or thrombin, whereas cobra venom is purely an antikinase.

One of the most important factors in the clotting of shed blood is the blood-platelets. It is generally held that they are one of the chief sources of thrombokinase, and that on chemical analysis they contain nucleo-protein, lecithin, and cholesterol. Many workers have suggested that lipoids (especially lecithin and kephalin) play an important part in clotting. A fact of significance is that kephalin is rarely completely free from calcium. There is some evidence that three substances play an important part in the formation of the clotting complex, viz. a protein, a lipoid, and calcium. Experiments to confirm this were carried out, also the preparation of an artificial calcium-lipoid mixture which had the properties of normal kinase, so far as the properties of this latter substance are known. One set of experiments showed that added lecithin had marked coagulative power in the presence of calcium. The calcium-lipoid combination does not yield calcium ions. Other experiments suggest that the lipoid is the most active substance in coagulation when combined with calcium. Also a protein seems to be necessary as a secondary factor, making the solution more sensitive, possibly by preventing the precipitation of the lecithin by the divalent calcium ion. Again, lecithin, in the presence of oxalate, can only cause clotting when it is combined with calcium. It can then adsorb oxalate in excess of the chemical equivalent of the calcium attached to it. Further experiments showed that lecithin, even in large amount, is unable to overcome the action of the hirudin in the absence of calcium.

Calcium itself is also unable to cause clotting in the absence of the added lecithin. The degree of coagulation is roughly proportional to the amount of lecithin contained in the added solutions. Thus lecithin can cause clotting in the presence of hirudin only when it is associated with ionized calcium. The same results were obtained on substituting cobra

venom for hirudin. The calcium-lecithin compound was relatively heat stable, the temperature at which activity is lost depending on the temperature of coagulation of the protein used. Solutions of this compound lose power in a manner similar to thrombokinase solutions when they are kept. This calcium-lipoid substance resembles the activated thrombokinase of Morawitz rather than the prothrombin of Howell. In the latter case, since the combination of prothrombin and calcium produces thrombin, if the calcium-lipoid substance were of this class it should give the reactions of thrombin. It does not do so, since it is not able to cause clotting in the presence of a large excess of oxalate, and its action is inhibited by cobra venom, which has no apparent action on thrombin. On the other hand, the work recorded seems to cast doubt on the identity of thrombokinase with a ferment. It is not at present possible to say whether the combination of calcium and lecithin is present as such in the circulating blood, or whether, when blood is shed, the ensuing physical changes cause the union to occur.

W. A. M. S.

Mas y Magro, M. Estudios sobre fisiologia de los tejidos linfoides. [**The physiology of the lymphoid tissues.**] *Arch. Card. y Hemat.*, 1921, **2**, 289–305.

Mas y Magro reports the results of a large series of animal experiments to determine the effect of injections of lymphatic gland extracts. The extracts were made up to 20 per cent. in normal salt solution with 0·5 phenol added. They were then heated to 45, 50, and 56° C. respectively on three successive days. The results obtained appear to Mas y Magro to justify the following conclusions. Lymphatic glands contain substances capable of inducing by injection hypertrophy of the germinative centres and circulatory lymphocytosis. They also contain substances inhibiting the cell-forming activities of the marrow. It is possible to produce a veritable status lymphaticus. The haemoclasic crisis of anaphylaxis is not altered by these extracts. Lymphocytosis with leucopenia, the characteristic finding in many endocrine disorders, is diagnostic of the hyperplasia produced by these extracts. This is a long and careful record, but it is questionable whether the results obtained by heated and carbolized extracts can be held to be true during life.

G. W.

Weber, F. Parkes. ***Polycythaemia, erythrocytosis, and erythraemia.*** [**B.**] London, 1921, pp. 148, price 21*s.*

The term polycythaemia embraces all the conditions in which the red blood corpuscles occur in numbers decidedly higher than the average. A count of 6,000,000 per c.mm. is not now regarded as pathological. A relative polycythaemia is the natural result of concentration of the blood from loss of fluid as in watery diarrhoea or persistent vomiting. In absolute or true polycythaemia the total number of red cells in the body is increased; as a rule the subject of it appears plethoric, and estimations show that the total quantity of blood in the body is also far above the normal.

Absolute polycythaemia may be divided into: (1) **Erythraemia**, a primary hyperplasia of the red cells, comparable with leukaemia; and (2) **Erythrocytosis**, a secondary hyperplasia of red cells, comparable with leucocytosis, resulting from imperfect oxygenation of the tissues. Stasis of blood in a large venous territory from cardiac or pulmonary disease or

from mechanical obstruction as by tumours will often induce not only a local but also a general erythrocytosis. Congenital pulmonary stenosis is another common cause. It follows residence in high altitudes, and the animal experiments and observations on this subject are examined by the author. Although the cause of the reaction of the bone-marrow in erythrocytosis is often evident, the cause of the primary hyperplasia leading to erythraemia is unknown. It is not here accepted as of a neoplastic nature.

In polycythaemia the viscosity of the blood is increased, yet the blood-pressure is not greatly raised nor the left ventricle much hypertrophied. Hypertonic polycythaemia is probably a separate group related to hyperpiesis or to granular kidney. Ayerza's disease is held to be a chronic cyanosis with secondary polycythaemia (erythrocytosis) of cardio-pulmonary origin. In many reported cases of erythrocytosis the circulatory changes can scarcely have been the cause, and in such there may be a chronic toxaemia in operation.

Erythraemia is due to a primary hyperplasia of the erythroblastic tissue of the bone-marrow. It was first clearly described by Vaquez in 1892 and 1895. 'Splenomegalic polycythaemia' is not always identical with it, for there are cases of the latter where splenic enlargement is incidental to the venous stasis from which the erythrocytosis arose. The symptoms are varied and include weakness, headache, vertigo, abdominal pain, and a tendency to haemorrhage. The vascular engorgement is not always so obvious as would be expected. The spleen is nearly always hard and enlarged so as to be definitely felt. Post-mortem examination of the bone-marrow supports the view of Dr. Parkes Weber that erythraemia is a primary myelopathy. Increased leucoblastic activity accompanies it, and certain cases even form a link with myeloid leukaemia. The splenic enlargement is partly due to engorgement and partly to hyperplasia of the pulp (? increased haemolysis). If the liver is enlarged in greater proportion than the spleen, the author counts it a point in favour of erythrocytosis rather than erythraemia. Thrombosis of abdominal vessels may complicate true erythraemia, but this should not on that account be confounded with erythrocytosis secondary to gross venous stasis or thrombosis. The author, like Dr. A. G. Gibson, in his recent lecture on chronic inflammatory diseases of the spleen, cannot accept splenic tuberculosis as a cause of erythraemia, though a degree of erythrocytosis occasionally results from it. No treatment has any uniform effect upon the disease; copious venesection often relieves the symptoms temporarily.

Detailed appendices furnish a complete account of the reported necropsies, and of numerous exceptional cases, published and hitherto unpublished. This book is a clear and concise yet complete monograph on the whole subject of polycythaemia. J. P.

Lustig, A., e Franchetti, A. Studi ed osservazioni sulla pellagra. [**Studies and observations on pellagra.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 187.

This is a long report prepared by Lustig as chairman, and Franchetti as secretary, of a committee set up by the Italian Home Office to study the new views on the aetiology of pellagra. After a most thorough investigation extending over four years, the committee came to the conclusion that the malady has an alimentary origin and is strictly related to feeding almost exclusively with maize. At present, however, it is impossible to

state with any degree of certainty whether pellagra is essentially due to the absence of an as yet hypothetical antipellagrous vitamin or to a complex of deficiencies comprising vitamins, proteic substances, mineral salts, &c. At any rate, maize is the chief responsible agent in the pathogenesis of pellagra, and it is logical to think that if sound maize is already so poor in principles essential for the nutrition of man, the poorer will it be when diseased and more or less unsuitable for consumption. C. d. F.

Azzi, A. (1). Sulla temperatura della mucosa tonsillare in condizioni normali e patologiche. [**On the temperature of the mucous membrane of the tonsils in normal and pathological conditions.**] *Riforma med.*, 1921, **37**, 175.

Azzi, A. (2). Azione degli stimoli termici cutanei sulla temperatura della mucosa della trachea e dei bronchi. [**Action of cutaneous thermal stimuli on the temperature of the mucous membrane of the trachea and bronchial tubes.**] *Riforma med.*, 1921, **37**, 509.

Continuation of investigations to which reference has already been made (see Viale, G., *Medical Science*, 1921, **3**, 371, and Azzi, A., ibid., **4**, 167, and **5**, 165). (1) The temperature of the mucous membrane of the tonsils may vary for various causes and independently of changes in the general body temperature. A mere quickening or slackening of the respiratory rhythm is sufficient to cause respectively a diminution or an increase in the temperature of the mucous membrane of the tonsils. In feverish conditions the temperature of the tonsillar surface varies independently of changes in that of the body. Thermal stimuli, even if applied to very small areas of the body surface cause noticeable changes in the temperature of the mucous membrane of the tonsils. (2) The same can be said as to variations in the temperature of the mucous membranes of the trachea and bronchial tubes. C. d. F.

Ferrata, A. Studi sulle emopatie. I. Sulla istogenesi della leucemia granulocitica. [**Studies on blood diseases. I. Histogenesis of granulocytic leukaemia.**] *Haematologica*, 1921, **2**, 242.

Investigations were carried out in sixteen cases of granulocytic leukaemia and led the author to the following conclusions: In the circulating blood and splenic tissue from patients with granulocytic leukaemia cells occur different from those already described by other authors, in normal or pathological conditions. These cells can be subdivided into three groups: (1) Indifferent cells of a lymphoid type provided with azurophil filaments and granules. (2) Cells similar to those of group 1, but with an initial intracytoplasmic differentiation of the azurophil filaments and granules into eosinophil or neutrophil granules. (3) Cells provided only with eosinophil or neutrophil granules. All of them have the following common characteristics: polymorphic shape, clasmacytoid or endothelioid aspect, nuclear chromatin arranged into a large meshed network (spongy nucleus). The nucleus of the cells of groups 1 and 2 possesses one or more nucleoli; the nucleus of those of group 3 has no nucleoli. The cells of group 1 can be considered as true granuloblasts in so far as they give origin, through a process of differentiation, to specific granulocytes. They may, therefore, be termed 'clasmacytoid or endothelioid myeloblasts', the names 'clasmacytoid promyelocytes' and 'endothelioid myelocytes' being suitable denominations for the cells of the remaining two groups. To indicate their origin the

adjectives 'histioid' or 'haemohistioblastic' can be used for all of them. As in the case of the normal bone-marrow those of the histioid myeloblasts, which will become transformed into either eosinophil or neutrophil myelocytes, can be recognized respectively by the thickness or thinness of their azurophil filaments or granules. Ferrata's paper is illustrated with nine coloured plates. C. d. F.

Cesaris-Demel, A. Sulle formazioni endoglobulari e sugli anelli di Cabot messi in rilievo nei globuli rossi normali colla ipercolorazione. [**On endoglobular formations and Cabot's rings shown in normal red blood corpuscles by overstaining.**] *Haematologica*, 1921, **2**, 125.

Boccadoro, C. Contributo allo studio delle alterazioni degli elementi del sangue in diversi stati patologici. [**On the alterations of blood corpuscles in various pathological conditions.**] *Haematologica*, 1921, **2**, 280.

Golgi, C. Il centrosoma dei globuli rossi del sangue circolante dell'uomo e di altri animali. [**The centrosome of red blood corpuscles of circulating blood of man and other animals.**] *Haematologica*, 1920, **1**, 333.

By means of a not as yet fully described modification of his bichromate and sublimate impregnation method Golgi has been able to show for the first time the unmistakable existence of a typical centrosome (centriole within a centrosphere) in the circulating red blood corpuscles of the adult man, children, human foetus, adult mammals, birds, reptiles, and amphibians. The opinion of the author on this important observation is summarized in the following sentence: 'Either the presence of a centrosome is taken to prove the persistence of a formative activity and in such a case the current opinion that the circulating red blood corpuscles are decaying elements destined to destruction is erroneous; or the circulating erythrocytes are actually cells which have reached the last phase of their evolution and in this case the significance generally attributed to the centrosome can hardly be admitted.' The dilemma will be solved only through further investigations.

By using the same method as Golgi, Boccadoro (one of his pupils) has found that in anaemias experimentally caused by means of blood-letting or poisoning with pyridin the centrosomes of both red and white circulating corpuscles appear increased in number and are more easily shown than in normal blood-cells. In the same and other pathological states Boccadoro has, in addition, observed that Golgi's reticulo-fibrillar body (see *Medical Science*, 1920–1, **3**, 368) is larger than in normal conditions.

The investigations of Cesaris-Demel were carried out by means of Neri's and Polettini's 'new-Giemsa', which have a staining power remarkably stronger than the usual Giemsa mixture. The results obtained are: The size of the circulating red blood corpuscles is approximately the same as that of the normoblasts from which they originate. This is due to the fact that the perinuclear layer of haemoglobin is homogeneous and very little retractile, so that it does not shrink when the nucleus of the normoblast disappears. At the same time and for the same reason the central portion rarefies and assumes, in the ripe erythrocyte, a spongy aspect. This central spongy portion can be easily shown in normal red blood corpuscles by overstaining. It is identical with the nucleoid endoglobular formations described by various authors under different names, as well as with Golgi's 'reticulo-fibrillar' body. By the use of hyper-colouring

mixtures one may also show that Cabot's ring-bodies are not a pathological but a normal occurrence, and that they probably are an appearance due to the staining of the internal rim of perinuclear haemoglobin, more dense in character than the central portion both before and after the re-absorption of the nucleus. These various facts support the view that red blood corpuscles are not homogeneous throughout. C. d. F.

BACTERIOLOGY

Topley, W. W. C., Barnard, J. E., and **Wilson, G. S. A new method of obtaining cultures from single bacterial cells.** *J. Hyg.*, 1921, **20**, 221.

Already a considerable number of methods exist for raising pure cultures from a single bacterial cell. All these methods, which are more or less difficult technically, aim at fishing out one single bacterium from a mixture and finally cultivating the progeny obtained by division. The present authors have devised an exceedingly ingenious method which aims at the destruction of all the bacteria except one which is protected during the process. The destruction is carried out by the sterilizing action of ultra violet light, the cell to be cultivated being protected from destruction by a small mercury globule 50 μ to 120 μ in diameter. The exact details of the method, which is of great interest to practical bacteriologists, must be consulted in the original. W. B.

Walker, E. W. Ainley. Studies in bacterial variability. On the occurrence and development of dys-agglutinable, eu-agglutinable, and hyper-agglutinable forms of certain bacteria. *Proc. Roy. Soc., Series B.*, 1922, **93**, 54.

It is a well-established fact that different cultures of an agglutinable bacterium may exhibit wide differences in agglutinability when tested with one and the same agglutinating serum. Hitherto it has been customary to speak of 'agglutinable' and 'inagglutinable' cultures. The author proposes a differentiation into eu-agglutinable, hyper-agglutinable and dys-agglutinable phases, and has shown that by repeated subculture in specific agglutinating serum diluted with bouillon dys-agglutinable forms were obtained with the following bacteria: *B. typhosus*, *B. paratyphosus* A and B, *B. aertrycke*, *B. enteritidis* (Gärtner), *B. coli*, *B. dysenteriae* (Flexner) V, W, and Z. On transference from the serum broth to ordinary broth these dys-agglutinable cultures yielded subcultures which were also dys-agglutinable. It was also found possible to raise hyper-agglutinable strains from an ordinary eu-agglutinable culture. In agglutination tests an excessively dys-agglutinable culture may fail to agglutinate at all with a serum which agglutinated the culture from which it was derived in a dilution of 1 : 1000 or more. It may also entirely fail to absorb from the serum any appreciable quantity of the agglutinins specific for that culture. Such results, in the opinion of the author, may necessitate a considerable change in the current views regarding the value of absorption tests as a means of determining bacterial affinities and may also throw light on the question of 'serological strains'. W. B.

Hitchens, A. P. Advantages of culture mediums containing small percentages of agar. *J. Infect. Dis.*, 1921, **29**, 390.

The author has investigated the growth of diverse aerobic and anaerobic bacteria on nutrient agar containing varying percentages of agar. He points out that 0·1 per cent. agar has two advantages as a culture medium over a medium containing higher percentages of agar. First, he claims superior anaerobic qualities, and, secondly, a greater luxuriance of growth of many bacteria and successful cultivation of certain species which only grow with difficulty or not at all on ordinary media. The explanation of the superior anaerobic conditions he concludes must be physical. On heating broth containing agar the latter goes into solution, on cooling the agar gels extruding a certain amount of broth. This gel consists of undisturbed films of agar, which, supported by the reducing action of the peptone and glucose, offers a barrier to the penetration of oxygen. He assumes that in the case of solid media the relations between the particles of agar and broth are modified by forces which act to destroy the continuity of the agar films. In addition to the absence of oxygen, growth is favoured by the thin consistency of the agar permitting ready extension of bacteria through it by development and motility.

The greater luxuriance of growth of aerobic bacteria on 0·1 per cent. nutrient agar, the author considers, is due to the fact that such medium is more similar physically to the body tissues, the agar gel taking the place of the cellular elements surrounded by the broth or body fluids.

G. T. W.

Brown, J. H. Hydrogen ions, titration, and the buffer index of bacteriological media. *J. Bact.*, 1921, **6**, 555.

The author commences with a discussion of the relative merits of titration of culture media, and of the determination of their hydrogen-ion concentration. He takes exception to the report on the Descriptive Chart of the Society of American Bacteriologists, that 'the titration method is entirely illogical for adjusting the reaction of media, or for determining the amount of acid produced by an organism'. Titration and hydrogen-ion determination tell entirely different stories. They are not simply two methods, one more accurate than the other, of determining the same thing. The titration method reveals facts not disclosed by a simple hydrogen-ion determination. For many common purposes a knowledge of the buffer content of media is quite as important as the hydrogen-ion concentration. The buffer content between stated limits of hydrogen-ion concentration is defined as the 'buffer index', which is the sum of the reserve acidity and reserve alkalinity between those limits.

A simple colorimetric method of determining these values is described. The determination can be easily and quickly made by any laboratory assistant. A copy of instructions for such an assistant is appended, together with a record of a sample titration.

W. A. M. S.

Wolf, C. G. L. The comparative influence of pure and commercial sugars and of combined and separate sterilization on bacterial metabolism. *Brit. J. Exp. Pathol.*, 1921, **2**, 266.

Four organisms, *B. coli*, *B. welchii*, *B. murisepticus*, and *B. tetani*, were examined to ascertain whether the purity of a sugar or the combined

sterilization of the sugar with the bouillon had an effect on the products of bacterial metabolism. The sugars used were glucose and lactose. While minor differences were encountered, these were not sufficient to indicate that combined sterilization or commercial glucose or lactose would influence a fermentation reaction sufficiently to lead to error. At the same time it must be remarked that with organisms more sensitive than those employed in the present study, or sugars more easily altered, it is quite possible that such errors could take place. P. F.

Airila, Y. Ueber die Bestimmung der Wasserstoffionenkonzentration im Gebiete P_H 8·45 – 10·5 vermittels einer Farblösungsreihe. [**The determination of hydrogen ions in the range P_H 8·45 – 10·5 by means of a series of coloured solutions.**] *Acta soc. med. fen.* '*duodecim*', Helsinki, 1921.

This is a consideration of the choice of indicators from the point of view of range and permanency of colour. For the range P_H 2·8 to 8·4, Airila advocates *o*-dinitrophenol, *p*-nitrophenol, and *m*-nitrophenol, whose tints remain unchanged for months. Between P_H 8·45 and 10·5, phenolphthalein is generally used. But unfortunately its maximum depth of colour remains unchanged only for one to two hours. For any measurement in this range one must make up a fresh series of tints daily. The author has endeavoured to find a more permanent set of tints which closely resemble those of phenolphthalein. He finds that a mixture of fuchsin and methyl violet in 95 per cent. alcohol is a great advance in this direction. He considers that, using these indicators with a Walpole comparator and matt surface, the colours can scarcely be distinguished from those of phenolphthalein. A 0·125 per cent. watery solution of fuchsin is prepared, and a saturated alcoholic solution of methyl violet diluted one thousand times with water. A table is appended showing the relation between the degree of colour and the P_H value of phenolphthalein. Then follow details showing how the colour test is to be carried out. W. A. M. S.

Hall, I. W. The P_H range for staphylococci. *Brit. J. Exper. Pathol.*, 1921, **2**, 242.

The general P_H range for the staphylococcal group extends from P_H 2·6 to P_H 10. But individual or group variations occur. These variations do not exhibit any relation to saprophytic or pathogenic characters. They do not admit of much experimental adaptation. The capacity for alkali production in sugar-free media is more evident in lower than higher P_H concentrations. By substitution of various acids in the acid series a limiting of the P_H range has been produced on the one hand and a definite acceleration of growth on the other, nitric acid being an outstanding adjuvant. P. F.

Fleischner, E. C., Vecki, M., Shaw, E. B., and **Meyer, K. F. The pathogenicity of *B. abortus* and *B. melitensis* for monkeys. Studies on the genus *Brucella nov. gen.*** *J. Infect. Dis.*, 1921, **29**, 663.

Since 1918 it has been shown by a number of American workers that *B. abortus* and *B. melitensis* are closely related morphologically, biologically, and serologically. The present communication deals with the behaviour of the two micro-organisms in the body of monkeys. Full data are given which show that virulent strains of *B. abortus* in sufficiently

large doses are pathogenic for these animals, although *B. melitensis* is far more invasive. Following an intravenous inoculation of *B. abortus*, agglutinins appear in the blood of monkeys and they may show an intermittent type of fever and lose weight. Infection may also be induced *per os*. W. B.

Oliver, W. W. Further observations on a rapid method of pneumococcus typing. *J. Infect. Dis.*, 1921, **29**, 518.

In a previous paper (*Medical Science*, 1920–21, **3**, 452), the author described his rapid typing method for pneumococci and the results obtained in 25 cases. He now records the results obtained in 100 cases examined by the same method controlled by other methods. In 100 consecutive unselected cases of pneumonia a typing of the pneumococcus was effected within 30 to 40 minutes in all but two cases by the rapid precipitin method, which was checked by the longer cultural or mouse method.

G. T. W.

Gordon, J. E. (1). The relationship of the pneumococcus to acute infections of the upper respiratory tract in man. *J. Infect. Dis.*, 1921, **29**, 437.

Gordon, J. E. (2). The Gram-negative cocci in 'colds' and influenza. *J. Infect. Dis.*, 1921, **29**, 462.

In the first paper are recorded the results of a study of two groups of cases, firstly, acute respiratory infections which come under the term 'common colds', and secondly, cases occurring in an epidemic of influenza. Cultures were obtained by means of a swab on a wire holder. Tests were made to ascertain the most favourable site for culturing, and it was found that the posterior nasal space was the region most commonly infected with the pneumococcus.

The method for demonstrating pneumococci was to culture the swabs for 8 to 12 hours in 5 per cent. sheep-blood dextrose broth and then to inoculate 1 c.cm. of the broth into white mice. Pneumococci isolated from the mice were then tested by agglutination and bile solubility. This method was found to be superior to blood-agar plates and picking off green colonies. Forty-six normal healthy persons were examined for pneumococci and 21·7 per cent. were shown to carry them. Nine out of ten of these strains fell into group 4, and were shown to possess a low grade of virulence. A series of 77 acute colds were investigated and 27 or 34·9 per cent. were shown to carry pneumococci. Here again type 4 preponderated over the others.

A small outbreak of sore throats in a school was investigated. Nine cases were examined over a period of three months at weekly or fortnightly intervals. A type 4 pneumococcus was isolated consistently from all nine patients throughout the course of the infection and for periods up to six weeks after clinical symptoms had disappeared. A number of normal throats in the same school were examined as controls and the particular type of pneumococcus was not obtained.

Thirty-seven cases of influenza have been examined. These were derived from three different sources. In these, three groups of pneumococci were shown to be present in 36 per cent., 33 per cent., and 50 per cent. respectively, and there appeared to be a fixed type in each group.

The numbers are, however, too small to warrant any conclusion. Experiments have been carried out to estimate the virulence of pneumococci derived from various types of cases. Pneumococci obtained from normal persons failed to cause death in mice within 72 hours. Pneumococci from cases of acute colds and from cases of influenza were shown to have a markedly higher virulence.

The author concludes that pneumococci are commoner in acute colds and influenza than in normals. Type incidence in these infections is not marked. A particular group in a localized epidemic, however, may show the uniform occurrence of a single type pneumococcus. The virulence of pneumococci in infections is greater than in normals.

In the second study Gram-negative cocci were investigated and an attempt made to determine their significance in common colds and in influenza. A preliminary investigation was made to determine the site at which Gram-negative cocci were most commonly present. It was found that the nasopharynx gave a higher percentage of positive cultures than the anterior nasal passages. Various media were tested and the highest percentage of positive results were obtained with oleate haemoglobin agar and with 5 per cent. sheep-blood agar.

About 250 Gram-negative cocci have been isolated from cases of acute colds, from influenza, and from normal persons. These strains have been grouped according to their power of fermenting a series of sugars. By this means 98 are shown to fall into the group *M. catarrhalis*, fermenting none of the test sugars. A further group of 100 strains ferment various carbohydrates and show chromogenic properties. *Meningococcus* was represented by 8 strains and *M. pharyngis siccus* and *Diplococcus crassus* by 20 and 15 strains respectively. The group *M. catarrhalis*, when examined as to its cultural characteristics, is not so homogeneous as would appear from the carbohydrate test. It is shown to fall into four subgroups by cultural differences.

The chromogenic group is subdivided into six subgroups by their fermentation reactions. The occurrence of these Gram-negative cocci in the various groups of persons examined is then given.

Of 110 normal people examined, *M. catarrhalis* was demonstrated in 51 while the other groups are represented less frequently. In cases suffering from a common cold 119 were examined and *M. catarrhalis* demonstrated in 54 cases. In 40 cases of influenza examined *M. catarrhalis* was present in 14. Tables of these three groups are given. Attempts were made to demonstrate differences in virulence of micrococci isolated from normal and from pathological conditions, but without success, the author concluding that there is no essential difference in the incidence of Gram-negative cocci in health and in disease. G. T. W.

Davis, D. J. The occurrence of hemolytic streptococci in the normal throat. *J. Infect. Dis.*, 1921, **29**, 524.

The author points out that whereas it is recognized that practically 100 per cent. of persons carry haemolytic streptococci in the tonsillar crypts or adenoid folds, it is sometimes considered that the percentage of normal individuals who carry haemolytic streptococci in the throat is not so high. In an examination of three batches of 15 individuals he shows that haemolytic streptococci could be isolated in all if three or four examinations are made in a period covering one month. G. T. W.

Bisbini, F. I bacilli piocianei in rapporto ai bacilli fluorescenti. [***B. pyocyaneus* in relation to fluorescent bacilli.**] *Ann. d'ig.*, 1921, **31**, 408.

B. pyocyaneus decolorizes in 2 to 4 days the bottom portion of agar tubes to which 4 or 5 drops of a watery solution of methylene blue were added. Later on the discoloured agar takes the colour proper to the strain of *B. pyocyaneus* used. According to the author this reaction is not obtainable by means of *B. fluorescens*, and other germs such as *B. coli communis*, *Streptococcus*, *Staphylococcus pyogenes albus*, *aureus* and *citreus*.

C. d. F.

Cook, M. W., and **Stafford, D. D. A study of the gonococcus and gonococcal infections.** *J. Infect. Dis.*, 1921, **29**, 561.

The object of this research was to devise improved methods of diagnosis of gonorrhoea and to determine whether strains of gonococci could be typed satisfactorily. After trying many media, testicular agar alone or containing blood or hydrocele fluid, gave the most luxuriant growths. Chocolate blood testicular agar was useful for invigorating poorly-growing cultures. Isolation of cultures from acute cases of anterior urethritis in the male was best obtained on chocolate blood testicular agar. No pure cultures of gonococci were isolated from five chronic cases of gonorrhoeal endocervicitis although micro-organisms similar to gonococci were found microscopically. The authors' results in attempting to type strains of gonococcus by complement fixation or agglutination tests were equally unsatisfactory.

W. B.

Thjötta, T., and **Avery, O. T. Studies on bacterial nutrition. III. Plant tissue as a source of growth accessory substances in the cultivation of *Bacillus influenzae*.** *J. Exper. Med.*, 1921, **34**, 455.

In previous papers (vide *Medical Science*, 1921, **4**, 387, 562; and 1921, **5**, 60) the authors have supported the view that two substances are essential for the growth of *B. influenzae*. The present paper deals with the nature of the 'X' substance. This is ordinarily found in blood-pigment, is heat stable and operates in minute amounts. The authors confirm the observations of others to the effect that the guaiac or benzidine reactions in blood derivatives go parallel with the power of these derivatives to induce growth and thus turn to vegetable tissues which also give these reactions as a source of their 'X' substance instead of blood.

They found that by placing a piece of sterile potato in ordinary broth *B. influenzae* not only grew quite well, but could be propagated from tube to tube indefinitely. Thus potato contains the 'X' substance. This substance is capable of resisting a temperature of 120° C. for 45 minutes, and thus in this respect resembles the 'X' substance of blood in being resistant to heat. It would appear that the authors consider that the 'X' factor of blood may be something entirely separate from blood-pigment. The same or a similar substance is present in vegetables and is presumably not the substance which is responsible for the benzidine test, since banana contains the 'X' substance but does not give the benzidine reaction. However, the authors do not profess to have advanced far with the identification of the substance. They opine that the high dilution in which it works suggests a catalytic action.

The authors' paper is of special interest in that it appears to clear up finally the question of the growth of influenza bacilli without blood and by a technique so simple that failure can hardly occur. P. F.

Maitland, H. B., and Cameron, S. C. A study of haemoglobinophilic bacteria by agglutination and agglutinin absorption. *Brit. J. Exp. Pathol.*, 1921, **2**, 283.

From the investigation of 38 strains of *B. influenzae* obtained from hospital patients during non-epidemic periods in Toronto, the following conclusions were made: (1) nearly all strains of *B. influenzae* possess a serological individuality as determined by agglutination and agglutinin absorption; (2) identical strains do occur, but they are not frequent; (3) the antigenic value of strains varies. Some are extremely narrow. The serum prepared from such strains agglutinated little more than the homologous organism; (4) the morphological variations are marked, but do not correspond to variations in agglutination; (5) two or more serological races may be present in the same patient. The results were in accord with those from other laboratories. P. F.

Rivers, T. M., and Kohn, L. A. The biological and the serological reactions of influenza bacilli producing meningitis. *J. Exper. M.*, 1921, **34**, 477.

The authors have made a comparative study of 13 strains of *B. influenzae* isolated by different workers during the last seven years. With one exception all the cultures produced indol, all reduced nitrates, all except one fermented glucose, fructose, galactose, and xylose, the exception being the same culture all through except in the case of the indol test. None of the 13 cultures fermented maltose. The 11 cultures which agreed culturally and biologically were found, however, by absorption tests to fall into two agglutinogenic groups with 7 in one and 3 in the other, one being intermediate. Two strains stood alone culturally and serologically. Four blood-culture strains from children with pneumonia differed from each other culturally and serologically, and when they showed a cultural relation to the meningococci races, this relation was not confirmed serologically. W. B.

Heller, Hilda H. Suggestions concerning a rational basis for the classification of the anaerobic bacteria. *J. Bact.*, 1921, **6**, 521.

This is a preliminary paper describing the views of the authoress as to how anaerobic bacteria should be classified. Up to the present the subject has been one of chaos. She does not believe that morphological criteria can be employed, but that a classification may be made on the basis of the chemical action of anaerobes upon carbohydrates and proteins. Pathogenesis and general morphology may be used as auxiliary generic characters. Specific differentiation of anaerobes may be based upon sugar fermentations, quantitative chemical action, morphology of colonies, and to some extent on the morphology of individuals. The authoress makes a tentative suggestion that the anaerobes should be classed in one family 'Clostridiaceae' of the order Eubacteriae. In this new family she distinguishes two sub-families: (1) Clostridioideae, and (2) Putrificoideae. Further details are promised in a later paper. W. B.

Perazzi, P. Sulla flora anaerobica dell' intestino dei neonati allevati al seno materno. [**On the anaerobic flora of breast-fed new-born infants.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 389.

The anaerobic flora of the intestine of breast-fed new-born infants appears between the tenth and twentieth hour, and does not contain any putrefying anaerobic germs during the first five days. During the first four days this anaerobic flora is formed by four well-defined species, viz.: (1) *B. perfringens* or a very similar variety; (2) germs of the group of *V. septique* of Pasteur; (3) germs similar to *B. III.* of Rodella and *B. sporogenes non-liquefaciens* of Jungano; (4) *B. bifidus* of Tissier, this last prevailing on the fourth and fifth day. C. d. F.

Amato, A. Ricerche sulla vaccinazione anticarbonchiosa con spore protette. [**Investigations on vaccination against anthrax with protected spores.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 327.

Spores of *B. anthracis* enclosed in small tubes of glutol (formolized gelatine) may be introduced into the subcutaneous tissues of extremely sensitive animals such as guinea-pigs in quantities much greater than the minimum fatal dose. Many animals survive, probably because the slow reabsorption of the gelatine tubes allows natural defensive powers to become strong enough to resist the infection. However, a true immunization of the guinea-pig against anthrax is very likely unobtainable. C. d. F.

Goss, L. W., Barbarin, R. E., and **Haines, A. W.** **Some characteristics of *B. chauvoei*.** *J. Infect. Dis.*, 1921, **29**, 615.

This paper deals with the differential bacteriological diagnosis of *B. chauvoei* from other anaerobes. It is particularly pointed out that on agar containing 2 per cent. of dextrose *B. chauvoei* fails to develop at all unless tissue or blood is carried over in the inoculum. This fact proved of great value in establishing the purity of the cultures, as the majority of bacteria found in emphysematous lesions grow well on the above medium. The pathogenic action of *B. chauvoei* is discussed, and it is pointed out that sheep are somewhat refractory to cultures. No strain of genuine *B. chauvoei* was isolated from the tissues of sheep dead from suspected 'black leg'. Protection tests with anti-black leg serum indicated a marked specificity for *B. chauvoei*. The diagnosis of this microbe by agglutination tests is considered by the authors as still in the experimental stage. W. B.

Wollstein, Martha. **Studies on the phenomenon of D'Hérelle with *Bacillus dysenteriae*.** *J. Exper. Med.*, 1921, **34**, 467.

The authoress examined the intestinal contents of 23 babies for the presence of d'Hérelle's so-called bacteriophage. Six of the children had a history of gastro-intestinal trouble and in one *B. shigae* had been isolated from the stools. Filtrates from the stools of 22 of the 23 cases showed no lytic action on young cultures of *B. shigae*. One lytic filtrate alone was obtained, viz. from a child dead from intussusception, and this filtrate was more active on *B. coli* than on *B. dysenteriae*. Experiments were also carried out on guinea-pigs inoculated intraperitoneally with *B. coli* and with *B. shigae*. The 'bacteriophage' obtained by inoculating the latter was

found to dissolve the homologous strain, five other Shiga strains, and two Flexner strains. On three strains of bacilli of Hiss Y type the action was less marked, while three strains of *B. coli* and one strain each of *B. typhosus*, *B. paratyphosus* A and B, *B. morgan*, *B. suipestifer*, *B. cholerae gallinarum* and *B. typhi murium* were not affected. The action of the lytic fluid on dysentery bacilli, both *in vivo* and *in vitro* is to divide the culture into sensitive and resistant strains, and the latter can be carried to a degree of very marked if not complete resistance to the lytic action. Plates poured from a fluid culture of *B. shigae*, which had been exposed to the lytic agent for 24 to 48 hours and which appeared to be completely dissolved, showed two kinds of colonies. One was round with regular edges, moist, and with a heaped up or denser centre. The other type was very irregular in size and shape, with deep indentations in its thin edges, a depressed centre, the whole colony being very granular. In broth the 'regular' colonies grew rapidly and produced a general turbidity, while the 'irregular' colonies grew more slowly and fell to the bottom of the tube in granular masses. The two different types of colonies did not, however, differ from the original culture in their carbohydrate reactions. The resistant strains were not lysogenic or agglutinable, whereas the strains sensitive to the action of 'bacteriophage' are agglutinable. Varying degrees of sensitive and resistant bacilli exist side by side in one and the same culture. The sensitive bacilli gradually lose the lysogenic property which they had acquired, but the very resistant bacilli never acquire that property. The lytic property of sensitive forms was found to be manifest in anaerobic as well as in aerobic conditions. Five excellent plates accompany this paper. W. B.

Ferro, P. Sulla resistenza e variabilità dei batteri del gruppo tifo-coli in mezzo nutritivo elementare. [**On the resistance and variability of bacteria of the coli-typhoid group in an elementary culture medium.**] *Pathologica*, 1921, **13**, 545.

Investigations were made by means of various strains of *B. typhosus*, *B. paratyphosus* A and B, and *B. coli communis*. As culture medium a 10 per cent. infusion of hay was prepared with tap-water and rendered slightly alkaline by the addition of a small quantity of a solution of potassium carbonate. By adding to this infusion 2·75 per cent. of agar-agar a solid medium was obtained. *B. typhosus* and *B. paratyphosus* A grew very badly on the elementary culture medium, but *B. paratyphosus* B and *B. coli communis* developed as on ordinary media. However, the four species equally maintained their morphological and biological characteristics.

C. d. F.

Mita, K. Dysentery-like diseases (paradysentery paratyphoid) in children and their causes. *J. Infect. Dis.*, 1921, **29**, 580.

During the last nine years the author studied several hundreds of dysentery-like cases in children in Fukuoka, Japan, and in 334 found dysentery bacilli of known types. In 73 cases he found organisms which he considers as hitherto unrecognized. Some resembled dysentery strains and he proposes to call the organism *B. paradysenteriae*, while others resembled paratyphoid bacilli and he proposes for these the name *B. paratyphosus* X. There appear to be two types of these paradysentery bacilli, 'A' and 'B', according as maltose and dextrin are decomposed in 24 hours (A), or not

after several days (B). Milk was coagulated after 2 or 3 weeks by freshly isolated strains. Saccharose and lactose were slowly decomposed by both groups. Mannitol and dextrose were split into acid in one day. Both types of paradysentery bacilli were agglutinated by the serum of patients up to a titre of 1 : 1000, but were unaffected by normal sera. The cultures were virulent for mice, guinea-pigs, and rabbits. Of the 73 cases from which paradysentery bacilli were isolated, 56 showed type A and 17 type B. The disease in children alleged to have been caused by these paradysentery bacilli was in general milder than true dysentery, but definite lesions were found in the large intestine. In addition to the above-mentioned paradysentery bacilli, the author found a micro-organism designated as '*B. paratyphosus* X' which forms acid and gas from mannitol and dextrose but does not affect saccharose, maltose, dextrin, or lactose. The account of the agglutinogenic reactions is meagre. A table is inserted giving the differential diagnosis of the types described. W. B.

Benians, T. H. C. Septicaemia: the selective deposition of the colon-typhoid group of bacteria in fixation abscesses. *Brit. J. Exp. Pathol.*, 1921, **2**, 276.

(1) Organisms of the colon-typhoid group, when embedded in mucilage, in the subcutaneous tissues of the rabbit or guinea-pig are protected from the defence mechanisms of the host, and may survive for some weeks. (2) These organisms, when directly inoculated with gum into the subcutaneous tissues, do not produce the intense local reaction with liquefaction of tissues that follows similar local infections with *S. aureus*. (3) These organisms are able to leave the vascular system without there being any gross mechanical lesion of the vessels. This facility of migration does not appear in the case of *S. aureus* and various other bacteria. (4) In experimental colon-typhoid septicaemia a subcutaneous fixation abscess of sterile gum tragacanth quickly becomes infected with these bacteria. Staphylococci on the other hand rarely gain access to the gum from the blood-stream. (5) It is suggested that the ready artificial infection of mucoid bodies by the colon-typhoid bacteria bears a close similarity to the infection of the mucous membranes of the body from the blood-stream as in the enteric fevers. It is not shown here whether bodies of this physical character receive the bacilli owing to a selective mechanism, or whether they merely favour their growth on account of the protection they afford them. (6) The transportation of the bacilli in these experiments apparently was not effected by phagocytes. P. F.

Kanai, S. Dysentery immunization in rabbits by the oral and subcutaneous methods. *Brit. J. Exp. Pathol.*, 1921, **2**, 256.

It has been possible to produce a certain small degree of immunity in rabbits by the oral administration of *B. dysenteriae* (Shiga). The immunity so obtained is found to be far inferior to that produced by the subcutaneous inoculation of a carbolized vaccine administered in three doses of 50, 100, and 100 millions. The oral administration of large quantities of killed dysentery bacilli to rabbits is without effect on their general condition as judged by the body-weight. P. F.

BIOCHEMISTRY

Carey, E. J. The experimental transformation of the smooth bladder muscle of the dog, histologically, into cross-striated muscle, and, physiologically, into an organ manifesting rhythmicity. *Am. J. Physiol.*, 1921, **58**, 182.

The argument underlying this paper is as follows: The normal differentiation of cross-striated muscle from the primitive undifferentiated mesenchyme is a gradual one and not a spontaneous act. The heart of the chick embryo begins pulsating about the 30th hour of incubation, but the structure of cross-striated muscle appears only at the 130th hour. Previously the heart structure is not unlike smooth muscle. The author argues that the appearance of cross-striation is the result of a protoplasmic reaction to the amount of work done by the cardiac mesenchyme. The tensional stimulus of the constantly increasing circulatory medium is therefore the extrinsic factor in the differentiation of cross-striated muscle. If this argument is correct, the smooth muscle of the bladder should eventually react by forming cross-striated muscle, and by manifesting rhythmicity, if the intravesicular hydrodynamic pressure and volume are increased in degree comparable with that found in the embryonic heart.

In order to test this hypothesis suprapubic cystotomy was performed in a four weeks old dog and a tube inserted. Through this tube warm concentrated boric acid was passed under varying volume and pressure conditions and at various intervals daily for 48 days, when the dog died of a uraemic toxaemia. The amount of fluid which could be passed through the bladder rapidly increased, so that at the end of the experiment the bladder passed 50,000 c.cm. of boric acid in ten hours of experimental observation. On the last day of the experiment manometric records were taken from the inlet tube of the bladder. These showed rhythmic beats when the bladder was distended and varying in rate with the distension. A regular rate of 65–75 beats per minute could be maintained. Histologically the thickened and hypertrophied bladder-wall showed red cross-striated muscle. This experiment proves then that function determines structure.

Unfortunately the histological evidence is presented entirely by microphotographs instead of drawings, which would be much more convincing. If the views of the author are correct, it is probable that a similar change would be visible in some of the numerous specimens of hypertrophied bladder stored away in pathological museums. W. C.

Schüller, J., u. Athmer, F. Über den Antagonismus der Lokalanästhetika gegenüber dem Veratrineffekt am Muskel. [**On the antagonism between local anaesthetics and the veratrin effect on muscle.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **91**, 125.

A muscle after immersion in a veratrin solution of 1 : 100,000 for five minutes shows the usual 'veratrin' response on stimulation, consisting of prolonged contraction and slow relaxation. If a muscle in this condition be immersed in novocaine (1 : 500) for 5 minutes, the veratrin effect passes off and the normal response returns. The action of the local anaesthetic has no relation to the nerve endings, for these may first be paralyzed by

curare. If then the muscle be soaked in veratrin, it will give the prolonged response typical of the action of this drug, and this again may be abolished by a local anaesthetic. J. H. B.

Weber, H. H. Die Lösung der Muskelstarre und die Beziehungen zwischen Quellung und Gerinnung des Muskeleiweiss. [**The resolution of rigor mortis and the relation between swelling and the clotting of muscle proteins.**] *Arch. f. g. ges. Physiol.*, 1921, **191**, 186.

The osmometer used in previous experiments was modified by using a collodion membrane, permeable for water and salts while practically or totally impermeable to protein. The conclusion of the previous work, that resolution of rigor is due, not to shrinkage of structural elements, but rather to bursting occasioned by accumulation of lactic acid, is confirmed. C. L. E.

Winterstein, H. Zur Kenntnis der Totenstarre. [**On rigor mortis.**] *Arch. f. d. ges. Physiol.*, 1921, **191**, 184.

Frog's sartorii kept in gaseous N_2 or H_2 show rigor in the usual way; if kept in O_2-free Ringer's solution no rigor develops, and lactic acid can be detected in the solution. This is a further proof that it is the accumulation of lactic acid which causes rigor. C. L. E.

Widal, F., Abrami, P., et **Brissaud, E.** Recherches expérimentales sur l'autocolloïdoclasie à frigore. [**Experiments on 'autocolloïdoclasie' produced by cold.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 207. (*Physiol. Abstr.*, 1921, **6**, 455.)

Dogs were exposed to cold by immersion in water at from 2° to 5° C. for varying periods. According to the length of time of immersion they suffered from manifestations of shock in varying degree. Short periods produced only a 'crise hémoclasique', consisting of (1) leucopenia, white cells diminishing in 45 mins. from 12,000 to 5,000; (2) increase of lymphocytes and decrease of polymorphonuclear cells; (3) large decrease in the clotting time of the blood; (4) diminution of the refractive index of serum. Further symptoms were pyrexia, dyspnoea, nausea, oedema, urticaria and finally haemoglobinuria. These symptoms are identical with those following intravenous injection of foreign protein into dogs, and with those of anaphylactic shock in the dog. These forms of shock would appear to be identical. The authors give the name 'colloïdoclasie' to the process involved. J. H. B.

Parhon, M. Sur la teneur en glycogène du foie et des muscles chez les animaux éthyroïdes. [**Content in glycogen of liver and muscles in thyroidectomized animals.**] *J. de physiol. et de path. gén.*, 1921, **19**, 198.

In lambs and guinea-pigs the total amount of glycogen in the liver is diminished after thyroidectomy, as is the percentage amount in the muscles. O. L. V. de W.

Glaubitz, G. Über Eiweisszerfall bei Vergiftungen. [B.] [**Protein destruction after poisoning.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 230.

The author has had the opportunity of studying cases in which carbon monoxide, oxalate, lysol, veronal, sublimate and bichromate, and pantopon were taken mostly with suicidal intent. A toxic destruction of protein was noted in both carbon monoxide, oxalate, lysol, sublimate, and opium. The hypnotics did not increase protein breakdown.

The self-administration of a large dose of pantopon by a chronic morphinist did not change the protein metabolism to any notable degree.

C. G. L. W.

Ellinger, A., u. **Heymann, P.** Die treibenden Kräfte für den Flüssigkeitsstrom im Organismus. I. Osmotische Wirkungen und Quellungsdruck der Eiweisskörper. [**The driving force for currents of fluid within the organism. I. The osmotic effect and force of imbibition of proteins.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **90**, 336.

Ellinger, A., u. **Heymann, P.,** u. **Klein, G.** Die treibenden Kräfte für den Flüssigkeitsstrom im Organismus. II. Quellungsdruck der Eiweisskörper und Diurese. Zur Wirkungsweise des Coffeins als Diuretikum. [**The driving force for currents of fluid within the organism. Imbibition pressure of proteins and diuresis. On the manner of working of caffeine as a diuretic.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **91**, 1.

These two papers furnish an important contribution to our knowledge of fluid interchange between the vessels and the tissues. The authors approached this subject in an endeavour to find an appropriate treatment for the lung oedema produced by gas poisoning during the war. After attempting to reduce tissue oedema by the injection of hypertonic solutions, in the hope that osmosis would cause the oedema fluid to be re-absorbed, a research was undertaken to investigate the adequacy of our present conceptions of the factors which underlie the passage of fluid in and out of the tissues.

Use was made of the hind limbs of the frog. These were each perfused through the artery, and the outflow collected from the vein. One limb was used as control. By admitting a known amount of fluid, and observing whether this was augmented or diminished in its passage through the limb, and by observing also whether the limb lost or gained in weight, it was possible to determine whether a perfusion fluid of given composition led to oedema formation, or conversely to a withdrawal of fluid from the tissues. The authors found that the effect of crystalloid solutions of different strengths was variable. A grape-sugar solution of so high a concentration as 25 per cent. did not lead to the withdrawal of water from the tissues. Both water and sugar entered the tissues. Very different was the effect of perfusing with a colloid. Thus it was established that perfusion with a dialysed serum which was chloride-free was equivalent to perfusion with a mixture of frog Ringer and water, the molecular concentration of which was such as to lower the freezing point by 0·18° C. Now this corresponds to an osmotic pressure of 1·2 atmospheres. Hitherto the function of colloid in controlling the passage of fluid from vessels to tissues has been considered limited to the exertion by the plasma protein of an osmotic pressure equal to 30 mm. according to Starling's measurement. A pressure of 1·2 atmospheres is obviously of a different order. However the colloids in the tissues are also

active, and it was found possible to increase their activity by the injection of more colloid, so that more water passed from vessels to the tissue spaces. It is therefore supposed that the exchange of fluid between vessels and tissues is not determined by a filtration pressure which has its origin in the blood-pressure, and by a serum protein osmotic pressure of 30 mm., as hitherto held. There is a balance between powerful forces of the plasma colloids on the one hand and of the tissue colloids on the other, the force being in the nature of a 'Quellungsdruck' or imbibition pressure. This is a particularly interesting conception at a time when the capillary pressure has been demonstrated by direct observation (Leonard Hill) to be no more than 2–5 mm., and therefore incapable of producing a filtration such as is demanded.

The second paper deals with the effect of caffeine on the imbibition power of the serum colloids. It was discovered that caffeine lessens this power and the suggestion arose that it was on these lines that the diuretic action of caffeine was to be explained. The experimental facts are (1) that the addition of caffeine to undiluted serum lessens the amount of water extracted from the tissues by the serum when this is perfused through the frog-leg preparation described above; (2) caffeine does not bring about this change by any effect on the permeability of the vessel wall, for the change is absent when a 25 per cent. sugar solution is substituted for serum; (3) caffeine in a dilution of 1 : 56,000 added to serum markedly increases the rate at which fluid can be filtered off from a mixture of serum and Ringer through a Bechhold ultra-filter. J. H. B.

Freund, H. Studien zur unspezifischen Reiztherapie. [**Studies on healing by non-specific stimuli.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **91**, 272.

In this paper an attempt is made to explain the changes which take place in the body after injections of various proteins which have been found to be beneficial in pathological conditions. It has been supposed that the changes are colloidal in nature, while an alternative theory considers that as a result of the protein injection there is an increased cell breakdown with the formation of certain substances in the blood.

Now Clark, in 1913, showed that serum could revive a frog heart which was exhausted by many hours' perfusion with Ringer. This restorative power was not due to the colloidal condition of the proteins, for it was possessed by an alcoholic extract of the serum. Since that time serum has been shown to possess various other properties; thus it can restore the beat of a frog heart stopped by muscarine; it can increase the effect of a digitalis solution; it has (*a*) vasodilator and (*b*) vasoconstrictor effects when perfused through the Läwen-Trendelenburg frog preparation. Freund now shows that all these effects are due, and due completely, to an alcohol-soluble constituent of serum, and not therefore to any colloidal configuration of the serum proteins. He next shows that the responsible substance is not present in the circulating blood of healthy animals. To do this it is necessary to collect blood direct from the carotid artery into alcohol; bleeding from the ear-vein (in the rabbit) is inadequate to demonstrate their absence. Finally, he shows that in rabbits suffering from coccidiosis, the circulating blood contains the substance in question; similarly, the blood of rabbits subjected to 'non-specific stimulus therapy' also contains it. Thus (1) after bleeding, (2) after the injection of caseosan, rabbit blood in circulation con-

tains an alcohol soluble substance which (1) can increase the action of digitalis; (2) can act like atropine on a muscarine-poisoned heart; (3) can cause (*a*) dilatation, (*b*) constriction when perfused through the vessels of a frog. The action on the frog vessels is interesting. If blood be withdrawn from a rabbit one hour after a caseosan injection, the alcohol soluble substance is purely vasodilator; but if it be drawn off forty-eight hours after the protein injection, the substance obtained is vasoconstrictor. The vasodilator substance is still there and may be demonstrated by the use of atropine. Freund supposes that the substance formed in blood as a result of this type of therapy is a product of cell breakdown, for Clark showed that a frog heart, perfused for many hours with the same small volume of Ringer, gave up to the Ringer substances which enabled it to revive another hypodynamic heart. J. H. B.

Bittorf, A. Über die Pigmentbildung beim Morbus Addisonii. [**Pigmentation in Addison's disease.**] *Deutsches Arch. f. klin. Med.*, 1921, **136**, 314.

By immersing strips of skin from cases of Addison's disease in dilute solutions of adrenalin darkening takes place. This is due to the oxidation of adrenalin, and the place of oxidation is in the epithelial cells of the skin. There is, therefore, an increase in oxydases in the pathological tissue.
C. G. L. W.

Camus, J., et **Roussy, G.** Syndrome adiposo-génital et diabète insipide expérimental. [**The syndrome of obesity and infantilism in relation to diabetes insipidus.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 296. (*Physiol. Abstr.*, 1921, **6**, 383.)

A dog, in which an experimental lesion at the base of the brain was produced at the end of 1919 has become enormously fat, while there are signs of testicular insufficiency. Its weight has increased from 15 to 26 kilos, and it suffers from diabetes insipidus, passing 3 to 4 litres of urine in 24 hours. J. H. B.

Cori, K. Untersuchungen über die Ursachen der Unterschiede in der Herznervenerregbarkeit bei Fröschen zu verschiedenen Jahreszeiten. Ein Beitrag zur Frage des peripheren Antagonismus von Vagus und Sympathikus und zur Beeinflussung der Herznerven durch Schilddrüsensubstanzen. [**Investigation on the cause of differences in the excitability of heart nerves in frogs at different times of the year. A contribution to the question of peripheral antagonism between vagus and sympathetic, and on the effect of thyroid on the heart nerves.**] *Arch. f. exper. Path. u. Pharmakol.*, 1921, **91**, 130.

Every teacher of physiology has long known that during the summer months stimulation of the vagus rarely results in stoppage of the frog's heart. This is now shown to be due to the fact that sympathetic fibres run together with the vagus, and in summer their excitability is increased, while that of the inhibitory fibres is depressed. The vagus effect can always be elicited in summer if the sympathetic terminations are first paralyzed with ergotamine. Or again, if a frog be taken in which vagus stimulation is followed by no inhibition, and a small dose of physostigmine be given, which by itself does not affect the heart-beat, stimulation of the vagus will then bring about typical inhibition. In winter vagal inhibition can normally be obtained on electrical stimulation of the nerve, but if a dose of atropine be given, the sympathetic effect can be demonstrated.

The change from the 'winter' response to the 'summer' response takes place at the breeding season. At that time it is common to find a frog which, while its own circulation is intact, gives an inhibitory response to vagus stimulation, but when its heart is perfused with Ringer shows a complete absence of inhibition. A frog which is selected at the time it is performing the sexual act always shows marked inhibition in response to vagal stimulation. Now thyroid extract has the property of abolishing an inhibitory response, that is to say, it has the property of increasing the sensitiveness of the sympathetic nerves and of diminishing that of the parasympathetic nerves. The author considers that there is a close relationship between the development of the thyroid in the summer months, and the changed response of the cardiac nerves. J. H. B.

Cori, Gerty. Experimentelle Untersuchungen an einem kongenitalen Myxödem. [**Experimental investigation of a case of congenital myxoedema.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 150.

The heat-regulating mechanism of a myxoedematous child of four years of age was compared with that of normal children of a like age. On placing in a cold bath the temperature of the former fell as much as 3° C. in the course of two hours and a half, while that of normal children was maintained, although both types of children showed external evidences of the cold bath.

In a warm bath the myxoedematous child did not perspire, and the skin remained white. It behaved as if narcotized. While the temperature of normal children rose, the temperature of the myxoedematous subject was unaffected by external heat. By the injection of foreign protein (3 c.cm. of cow's milk) there was a rise in temperature amounting to over 2° C. Pilocarpine and atropine exercise a more pronounced effect than with normal children.

The child was treated with thyroid with evidently excellent effect (photographs) and the experiments repeated. In all cases, as shown graphically by charts, the metabolism approached that of normal children. It is noteworthy that in the myxoedematous condition the child did not react to adrenalin with a glycosuria. C. G. L. W.

Nees, F. Über die lipolytische Tätigkeit der weissen Blutkörperchen. [**The lipolytic action of leucocytes.**] *Biochem. Ztschr.*, 1921, **124**, 156.

By the use of wax plates made from mixtures of beeswax, lard, &c., it has been possible to demonstrate fat-splitting ferments in leucocytes and and lymphocytes. The former ferments are less resistant to high temperature than those of the lymphocytes. C. G. L. W.

Forssman, J. Zur Chemie der Wassermann-Reaktion. [**The chemistry of the Wassermann reaction.**] *Biochem. Ztschr.*, 1921, **124**, 185.

The author had previously shown that the reacting substance in syphilitic serum, when precipitated with the globulins and treated with ether after solution in soda, lost its power of deviating complement. He therefore concluded that the reacting substance was soluble in ether. Further experiments described in the present paper have modified his views. The inactivation was due to minimal amounts of ether retained. It would appear that the sensitiveness to ether which the Wassermann body possesses is probably due to the change in the dispersion of the substance rather than in a solubility in ether. C. G. L. W.

Schachenmeier, H. Beitrag zur agglutinogenen Wirkung der Bakterienfette. [**The agglutinin formation by bacterial fats.**] *Biochem. Ztschr.*, 1921, **124**, 165.

By isolating fats from *B. typhosus*, staphylococci, and *B. coli*, and purifying them so that they gave no reaction with the ordinary protein reagents, it was possible to prepare emulsions which, when injected into men and rabbits, produced specific agglutinins. In only one case was there a local and thermal reaction. Agglutinations at 1–1280 were obtained. A certain amount of coagglutination was also observed. C. G. L. W.

Dernby, K. G., u. **Allander, B.** Studien über den Einfluss der Wasserstoffion enkonzentration auf das Wachstum und die Toxinbildung der Tetanusbacillen. [**Studies upon the influence of hydrogen-ion concentration upon the growth and the toxin formation of the tetanus bacillus.**] *Biochem. Ztschr.*, 1921, **123**, 245.

In this study it is shown that the tetanus bacillus grows best at about the reaction of the blood, though it will grow between the limits of reaction P_H 5–8·5. Tetanus toxin is only stable within narrower limits of reaction, viz. P_H 5·8–8. It is destroyed in acid media which will support the life of the bacillus. This means that for a mass production of the toxin during growth the reaction of the medium must be kept slightly upon the alkaline side of the neutral point. R. A. P.

Storm van Leeuwen, W., and **von Szent-Györgyi, A. On the influence of colloids on the action of non-colloidal drugs.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 271.

The authors have already shown that rabbit serum contains substances which have the property of inhibiting the action of atropine and pilocarpine. These experiments, done in Utrecht, could only be repeated partially when performed in Leyden. In searching for the cause of the discrepancy they found that in the former place the blood had been taken from animals previously etherized, while in Leyden the blood was withdrawn without this anaesthetic. They have tested this point and find that the fixing power of serum for pilocarpine can be inhibited by the action of chloroform, and more especially ether. Other substances such as peptone have a similar effect. These observations fit in with the fact noted by Dale that histamine is ten times more poisonous for the cat when it is narcotized. The authors look on the phenomenon as an action of the narcotic in shifting the colloidal qualities of the serum in a direction in which the colloids have less capacity for fixing a poison. It is obvious that if this be so a large field is opened up in the study of shock in the anaesthetized subject. It is hoped that the work may be extended to a study of nitrous oxide, which is well known to produce less shock than other anaesthetics. C. G. L. W.

Benedict, Francis G., and **Hendry, Mary F. The energy requirements of girls from 12 to 17 years of age.** *Boston M. & S. J.*, 1921, **184**, 217, 257, 282, 297, 329. (*Chem. Abstr.*, 1921, **15**, 3644.)

The average minimum resting pulse-rate per minute of girls from 12 to 17 years of age, just before arising in the morning, was found to be 81 at 12, 77 at 13, 77 at 14, 83 at 15, 71 at 16, and 74 at 17 years. The

insensible perspiration for these girls per kilogramme body-weight per hour was as follows : 0·72 gm. at 13, 0·71 gm. at 14, and 0·77 gm. at 15 years. The respiratory quotient of groups of 12 girls each, about 7–8 hours after a light meal, were 0·81, 0·81, 0·78, and 0·79. The calorific requirement of young girls during 10 hours of bed rest was, on the average, 55 calories per individual per hour. The average 24-hour basal heat-production of girls from 12 to 17 years of age was 1,250 calories per individual, irrespective of age. The heat-production per kilogramme body-weight per 24 hours decreases regularly with increasing age from 29·9 calories at 12 years 2 months to 21·7 calories at 17 years. The curve indicating the general metabolic trend is throughout its entire length materially below the few scattered observations of earlier writers. The heat-production per square metre of body surface per 24 hours likewise decreases, but not so regularly, with increasing age, ranging from 928 calories at 14 years to 745 calories at 16 years. The metabolism of groups of young girls can be predicted from the general curve, indicating the heat-production per kilogramme of body-weight referred to age within an error of 3·1 per cent. The heat prediction for the heat-production per unit of body-weight is somewhat better than that per unit of surface area. The curves representing the heat-production per kilogramme of body-weight and per square metre of body surface referred to weight for these groups of girls from 12 to 17 years of age blend with remarkable uniformity with similar curves based upon the measurement of a large number of normal girls from birth to 12 years of age. No influence of puberty or the prepubescent stage is clearly proved in any of the results. C. G. L. W.

Muggia, Alberto, and Gasca, Enrico. Vegetable milk of the soy bean in alimentation and in the therapy of gastro-enteric diseases of infants. *Gazz. d. osp.*, 1921, **42**, 356. (*Chem. Abstr.*, 1921, **15**, 3511.)

A suspension of soy-bean flour can be prepared which is stable, and which has a nutritive value closely approaching to that of cow's milk. Comparative analyses are given. To prepare a litre of 'vegetable milk', 150–160 gm. of the beans are steeped in tepid water for 12–24 hours, which causes considerable swelling. They are then carefully crushed; 1 litre of water is added, little by little, and the whole then boiled 15 minutes, and filtered through sterilized gauze, forming a white emulsion. If the taste is not agreeable it can be improved by the addition of a small amount of real milk. The suspension coagulates under much the same conditions as real milk, and similar precautions in its handling must be observed. Figures are given showing marked improvement and gain in weight of infants in whose diet the suspension was substituted wholly or in part for true milk. This was especially noticeable in gastro-intestinal disorders, or where human or cow's milk was not well tolerated. 'What is most important, from our point of view, is that the soy-bean milk, in the cases observed by us, shows itself to be more easily tolerated than the milk of animals, and sometimes more easily than human milk. The experiments will be continued on a larger scale and under more exact biochemical control, and we believe that we shall be able to show that in many affections of the digestive system of infants where there is evidence of intolerance toward animal milk, we shall be able to substitute the soy-bean milk wholly or partially, not only without inconvenience, but with improvement in the local condition of the digestive

organs, and improved general condition of the child.' The use of soy-bean flour in preparing food for diabetics, industrial uses of the oil, and of the 'vegetable casein' are also suggested. References to the literature are given. C. G. L. W.

Griffeth, J. P. Crozier, and Mitchell, A. Graeme. Some remarks on the elements of diet in infancy, with special reference to the employment of Czerny and Kleinschmidt's butter-flour mixture. *N. York M. J.*, 1921, **114**, 137. (*Chem. Abstr.*, 1921, **15**, 3511.)

The authors review in part the literature concerned with the digestion and action of the different ingredients of the infant's diet, and particularly the reports having to do with the feeding of the Czerny-Kleinschmidt butter-flour mixture (*Jahrb. Kinderheilk.*, 1918, **87**, 1). Their results lead to the conclusion that the feeding of this mixture to infants often results in a better fat tolerance of the subjects than can be obtained by any other known method; and that they indicate a strong proof of the great need of the infant economy for a food sufficiently high in fat. C. G. L. W.

Ryffel, J. H. The chemical estimation of gastric function by the test meals of Ewald and Boas. *Lancet*, 1921, i, 586. (*Chem. Abstr.*, 1921, **15**, 3295.)

Different indicators have been used to determine gastric acidity. Total acidity is usually determined by titration with NaOH, with phenolphthalein as indicator. The earliest indicator for free HCl was that of Günzburg. This has been shown to give results comparable with those of physical measurements, but as the test involves evaporation it is not convenient for purposes of titration. Töpfer introduced dimethylaminoazobenzene, which has been widely used, but the region of change for this indicator lies between N/1,000 and N/10,000 HCl, and the end-point as ordinarily employed about N/5,000 HCl, which is distinctly too low in the acid scale for a determination of free HCl. Although the term 'free HCl' in this connexion is a misnomer, the indicator is of great utility, as organic acids produced by the Oppler-Boas bacillus and acid streptococci never attain, either in the stomach or in culture, in the presence of sugar, an acidity great enough to affect dimethylaminoazobenzene, so that the titration is not affected by organic acids. Rolph proposed to use instead tropeolin 00, which reacts at N/200 HCl, while recently Cole and Adie have urged the use of thymol blue working to an end-point = HCl, $N \times 10^{-2 \cdot 6}$, or about N/500. This indicator would leave a large gap between the total acidity and the free HCl, so that it would surely be better to retain dimethylaminoazobenzene, and, in addition, add a suitable indicator to the filtrate to compare the tint obtained with a series of tubes containing known quantities of HCl, so as actually to determine the concentration of H-ions present. B. Moore employed the rate of hydrolysis of methyl acetate to determine the free HCl. The method is sound physically, but somewhat laborious. Willcox developed the determination of a quantity of a different kind, the 'active HCl'. This is based on the method originally employed by Prout to demonstrate the presence of free HCl in gastric juice. It is essentially a determination of the loss of Cl on ignition, and includes free HCl and HCl combined with proteins and other volatile bases. Active HCl corresponds closely with the result of titration of total acidity unless organic acid be present, when the

difference between the two measures the organic acid. Graham pointed out that the estimation of mineral, or non-volatile Cl, which is involved in the estimation of active HCl, was itself of value, as this quantity was notably increased in carcinoma of the stomach and in regurgitation of duodenal contents into the stomach. In test meals of the type described there are two principal sources of error: if the stomach empties quickly, as it frequently does in cases of duodenal ulcer, a small amount of material is obtained, which is rich in mucus, poor in toast, and contains HCl less than normal and a high mineral Cl. The remedy is to shorten the time, so as to obtain a true sample of the meal. The other source of error is that aspiration is liable to cause some bleeding; there the remedy is to insist on the examination of the faeces for blood in every case. If the blood in the test meal is due to trauma it will not be found in the faeces. Spectroscopic examination is also desirable. The fractional test meal gives results that are of great interest, but it serves rather for arranging the cases in various groups than for individual diagnoses. C. G. L. W.

Hess, W. R. Die Rolle der Vitamine im Zellchemismus. [**The rôle of vitamins in the chemical processes of the cell.**] *Ztschr. f. physiol. Chem.*, 1921, **117**, 284.

The condition of avitaminosis in pigeons is due to a reduction of the enzymes responsible for tissue respiration. It has been shown *in vitro* that tissues taken from birds in this condition display diminished respiration. The typical symptoms of avian beri-beri can be reproduced accurately by prussic acid poisoning, which reduces tissue respiration. H. W. D.

Downs, A. W., and **Eddy, A. B. Secretin V. Its effect in anaemia, with a note on the supposed similarity between secretin and vitamin B.** *Am. J. Physiol.*, 1921, **58**, 296.

The authors have shown previously that the subcutaneous injection of secretin increases the red blood-cell count in rabbits. This is very marked when an anaemia is previously produced by keeping the rabbits on a diet of polished rice which is free from vitamins. The injection of secretin produces then an increased rate of blood regeneration and increased ability to put on weight. This improvement is greater than can be obtained by dietary adjustment alone. But secretin is not identical with vitamin B (confirmation of Drummond and Anrep). W. C.

Mollow, W. Milz und Verdauung. [**Spleen and Digestion.**] *Ztschr. f. physiol. Chem.*, 1921, **117**, 218.

Contrary to text-book statements, the author finds that the spleen exercises no influence whatsoever on the digestive organs. H. W. D.

Burton-Opitz, R. The venous supply of the heart. *Am. J. Physiol.*, 1921, **58**, 226.

The various factors determining the venous supply of the heart are subjected to an experimental and critical examination in this extensive paper. The experiments were made in cats. The main results will be given briefly under the different headings.

(1) **Effect of occluding parts of the pulmonary circuit.** The com-

pression of the pulmonary vessels of one side gives rise to a decided reduction in the venous supply of the heart, a rise in the venous pressure, and a fall in the carotid pressure.

(2) **The effect of varying degrees of ventilation in the lungs.** All degrees of lung ventilation exceeding the normal expansion produce the same effects as those described under (1). The venous supply of the heart and its output is therefore markedly affected by the activity of the lungs (contrary to the view of Tigerstedt). Simple collapse of one lung does not seriously impair the blood-flow through the lungs, and does not reduce the venous supply of the heart. A clear distinction should therefore be made between a lung in a state of simple collapse, which still possesses a considerable vascularity, and a lung the vessels of which have been ligated.

(3) **Partial and total compression of the pulmonary artery.** This also produces a reduction in the venous return, rise in venous pressure, and fall in carotid pressure, but the changes are greater than those produced by compression of the vessels of one lung. A moderate stenosis down to one-half the normal lumen is readily compensated. A failure of the circulation does not set in until the stenosis is so severe that the size of the pulmonary orifice has been diminished to about one-fourth of normal.

(4) **The effects of tricuspid regurgitation.** This was produced experimentally by means of a specially constructed cannula, and the condition induced corresponds to that of lost compensation in the human heart. There is a rise in venous pressure with a decrease in the blood-flow of the vena cava and a fall in carotid pressure.

(5) **The effects of aortic stenosis and mitral insufficiency.** The observations under this heading refer to the immediate effects produced by compressing the aortic orifice. They correspond in main to the changes arising during decompensation. There is a rise in caval pressure, a reduction in the venous supply of the heart, and a fall in carotid pressure. These effects do not assume a serious character until the constriction has caused a reduction in the size of the aortic orifice to about one-half of normal. While aortic stenosis must be severe before circulatory changes set in, mitral insufficiency, induced experimentally by means of the special cannula mentioned above, produces disturbances more readily. These changes are a retardation of flow through the lungs and a decrease in the output of the right ventricle, as revealed by a diminution of the venous inflow into the right ventricle and a rise in the caval pressure.

(6) **The effects of compression of the vessels of the head upon the blood-flow in the inferior vena cava.** Compression of the arteries of the head and forelegs produces marked rises in the arterial pressure (measured in the femoral artery) and in the venous pressure (measured in the inferior vena cava). There is a greatly increased blood-flow in the latter vessel.

(7) **The effects of compression of the thoracic aorta upon the blood-flow in the inferior vena cava.** After the ligation of the thoracic aorta the inferior vena cava still carries an appreciable quantity of blood, which becomes increasingly larger as the level of compression is moved towards the diaphragm. This confirms the existence of an anastomosis in which the intercostal arteries participate.

(8) **The blood-flow in the superior vena cava during the occlusion of the thoracic aorta.** The circulation through the vessels of the head and legs is greatly increased.

(9) **The effects of stimulation of the greater splanchnic nerve and of the central end of the divided sciatic nerve.** The chief interest of this section lies in the confirmation of Cannon's view that the circulatory changes observed are due to a secretion of adrenin, and not, as Stewart and Rogoff maintain, to a redistribution of the blood.

Average diameter.		Velocity per second.	
Inferior vena cava.	Superior vena cava.	Inferior vena cava.	Superior vena cava.
7·9 mm.	5·2 mm.	122·4 mm.	170·7 mm.

(10) **The volume and velocity of the blood-flow in the venae cavae.** The superior vena cava accommodates less than three-fourths of the quantity of blood present in the inferior vena cava. This relationship is the reverse of that obtaining before birth. The heart of a cat of medium size (4–4·5 kgm.) receives about 3 c.cm. of caval blood during each diastole.

W. C.

Lifschütz, I. Zur Kenntnis der chemischen Natur und der Wandlungen des Blutfettes. [**Contribution to the knowledge of the chemical nature and changes of blood fat.**] *Ztschr. f. physiol. Chem.*, 1921, **117**, 212.

An examination of the fat of two specimens of ox blood leads the author to conclude that the cholesterin of the blood arises from the oxidation of oleic acid present in the blood fat. H. W. D.

RADIOLOGY

Radiotechnique

Wels, P. Untersuchungen über die Brauchbarkeit des Sabouraud-Dosimeters. [**Investigations as to the usefulness of the Sabouraud dosimeter.**] *Strahlentherapie*, 1921, **13**, 174–96.

The result of these inquiries is that when tested by iontoquantimeter readings the pastille has a very considerable value and accuracy, especially when filters of 4 mm. Al or over are used if the source of the current shows considerable fluctuations. Mayer's method of pastille estimation is used, which the author considers much more reliable than Holzknecht's, upon which Krönig and Friedrich's unfavourable opinion of the pastille was based. For each apparatus and filtration the erythema dose should be compared with the Sabouraud dose, and then all doses can be given as fractions of the erythema dose. In addition, the scattered radiation which affects the skin from below, and may amount to 30 per cent. of the direct dose, depending on the radiation quality, filter, area of the irradiated field, and the thickness of the part should be estimated; small fields and thin regions of the body lead to under-dosage, if this factor of scattered radiation be not taken into account. J. H. D. W.

Radiodiagnosis

Ström, S. On the X-ray diagnosis of changes in the appendix and caecum. [B.] *Acta Radiol.*, 1921, **1**, 133.

The author deals with 110 cases, 50 of which, having had no clinical or subjective sign of affection in the appendix region, are regarded as normal cases. The technique is described at length. Barium sulphate is used, and the method of preparing the meal is given. Stress is laid on the point of examining the stomach and duodenum as well as the appendix area: the first examination of the latter should be made 6–7 hours after the meal. The appendix is most often filled 8–9 hours after the meal. Difficulties as regards seeing the appendix are gone into, and with regard to this it is pointed out that each case must be examined individually; fixed hours are impossible. In many cases an enema examination is made to finish the X-ray examination. The patient is always recumbent and the trochoscope used. The variations in the position of the caecum are next dealt with and three cases cited as illustrations of some points. In answering the question as to how often the appendix is visible at an X-ray examination the author states that in his normal cases it was seen in 50 per cent., and in the pathological cases in rather more than 75 per cent.; in the great majority of cases where the appendix was not seen the caecum was in the lesser pelvis and could not be moved up. The normal positions of the appendix are enumerated, also the shape and size; from the latter it is pointed out that a wide lumen cannot be credited with any pathological importance. The contractions of the appendix and of the caecum play a great part in filling the appendix; these contractions and the wave-like movements of the appendix are described. The normal appendix empties 1–2 days after the caecum, but if very long may take up to five days without being in any way pathological.

The pathological appendix. Little is known of the appearances in acute appendicitis, as practically no opportunities for examination have occurred. Under this heading the author deals with 26 cases which were operated upon, and in 22 of these the diagnosis was confirmed. In every case except one the appendix was seen under the screen. 1. *Stenosis of the appendix.* A description is given of stenosis occurring in different parts of the organ; three cases are described. 2. *Kinks and adhesions.* If the kink does not cause stenosis the appendix fills well; as regards adhesions, it must be remembered that the appendix is in most cases relatively immobile. Three cases are described. 3. *Hyperperistalsis, spasm.* To illustrate this four cases are described. 4. *Faecal concretions, faecal lumps, and foreign bodies in the appendix.* Lime-encrusted concretions are rare; usually the concretion consists of intestinal contents and products of the appendicular mucosa which do not form a shadow, but show as light gaps if the appendix be filled with the opaque meal. According to one author quoted a hook-shaped end to the shadow of the appendix should suggest a concretion. 5. *Tenderness on pressure and reflex symptoms in the stomach.* The author states that X-ray examination alone can localize tenderness in relation to the various organs. Only in conjunction with changes in form of the appendix, &c., is tenderness of any diagnostic value. 6. *Inflammatory changes in the caecum in appendicitis.* This may represent an ileo-caecal tumour; a case in point is described.

The incompetency of the ileo-caecal valve. Opinion as to the importance of this is divided; according to the author it is not a pathological sign, especially if it has been observed only after an enema, in which case the valve is not under physiological conditions. To prove incompetency, according to the author, a barium meal must be seen to pass backwards from caecum to ileum. He does not deny that the condition may be of pathological importance, but asserts that it cannot be interpreted as an inflammatory process in connexion with chronic appendicitis.

The paper is completed with twenty-four excellent skiagrams which are fully explained, and refer to the cases mentioned in the text.

P. L.-B.

Melville, S. Some points in the diagnosis of hilum tuberculosis in the adult by means of X-rays. *Arch. Radiol. & Electroth.*, 1921, **26**, 178.

The author begins by saying that serious research for linking up clinical with radiographic and pathological findings is urgently needed. Five conditions which can give rise to exaggeration of the hilum or peribronchial shadows, and so lead to erroneous diagnosis of hilum tuberculosis, are given. The highly-skilled percussion needed to diagnose hilum tuberculosis is, in the author's opinion, limited to very few persons, and he asserts that radioscopy can aid diagnosis very greatly, and is not valueless, as some physicians assert. A description of the X-ray picture and of the technique is given. Great stress is laid on marked narrowing, and lessened expansion at the apices of both lungs. P. L.-B.

Gallus, H. Über Spondylitis typhosa. [**On typhoid spondylitis.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 13.

In dealing with the subject of typhoid spondylitis Dr. Hermann Gallus opens his article by detailing the special symptoms by which the typhoid variety may be distinguished from other forms of spondylitis. (1) The unusual strength of the widespread area of the pain. (2) The visible swellings of the softer parts. (3) The acute run of fever. (4) The speedy disappearance of the spinal symptoms.

He calls attention to the fact that as long ago as 1894 Quincke showed that typhoid bacilli are found in the bone-marrow of typhoid patients as constantly as in the spleen.

In an exhaustive account of a case of a 17-year-old patient who came to the hospital after an illness of three months' duration complaining of pain in the lumbar regions, cough with expectoration, headache, and great weakness, he states that at first the diagnosis was lumbago. As, however, it did not yield to treatment, and as the patient had not had typhoid fever previously, but attributed his condition to an attack of influenza, radiological examination was made and revealed changes indicating typhoid spondylitis. In the left half of the third lumbar vertebra there was strong indication of loss of bone-structure; on the under surface of the same vertebra there were small projections of bone, also on the under surface of the second lumbar vertebra on both sides, but more marked on the left, there were similar changes. The appearance of an enlargement of the spleen indicated typhoid infection, and examinations of the blood and stools were made, but with negative results. Repeated Widal tests gave markedly

positive results in high dilutions with the typhoid bacillus, but not with paratyphoid organs.

Injections of typhoid vaccine at first proved ineffective, but after the second injection there was a rise of temperature, and after the third week the patient was convalescent and the changes in the spine had almost disappeared. In conclusion, the writer states that although the ordinary typhoid symptoms were lacking, yet the Widal reaction and the results of the subsequent injection of the vaccine clearly indicated typhoid bacilli in the bones of the vertebrae. F. E. R.

Kohlmann, G. Zur Klinik und Röntgendiagnose der multiplen Myelome. [**On the clinical and Röntgen diagnosis of multiple myeloma.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 26.

Myeloma, or Kahler's disease, as it is also known, is so infrequent that its diagnosis has been surrounded with difficulties, in as much as it has been mistaken for osteomalacia.

The symptoms of the disease, from instances given by the author, are by no means similar in each case, nor is the period of development the same, the duration of the illness varying from a few months to eight years. Myeloma, the author states, is spread fairly evenly all over Europe, chiefly attacking men of mature age, although women are by no means exempt; he records three cases of patients aged 46 and 47 respectively, and one woman of 56.

Despite the difficulties attending the correct diagnosis of multiple myeloma, Kohlmann claims to have found certain strongly differentiating symptoms, which he considers should more or less easily facilitate its distinction from osteomalacia.

(1) Osteomalacia never attacks the bones of the skull; myeloma frequently does so.

(2) In osteomalacia the pelvis takes a heart-shaped form and the sacrum becomes considerably bent in; in myeloma none of these changes are observable, the pelvis and sacrum retaining their normal shape.

(3) Osteomalacia shows an extensive, uniform deterioration into brittle chalky substances, which give light shadows in X-ray pictures; multiple myeloma only numerous round reflections, pointing to groups of bone defects caused by tumours.

(4) Osteomalacia reveals a tendency to curvature of the long bones, and, as in rickets, the form changes, while in myeloma the bony contour seems unchanged, but there is a tendency to spontaneous fracture, especially of the ribs, with decided S-shaped curvature of the sternum.

(5) Osteomalacia attacks women of varying ages, myeloma, chiefly men over forty.

(6) Bence-Jones's albumose is absent in osteomalacia, but almost always appears in myeloma.

(7) Parchment-like crepitations are observable in myelomas, particularly in the ribs and sternum, but not in osteomalacia.

(8) Finally, the extraordinary and rapid loss of weight in patients with myeloma is never so noticeable in osteomalacia.

All these points Kohlmann claims as being decisive in diagnosis; nevertheless he adds that even amongst these there may be variations which raise difficulties, as, for instance, points (1) and (2) are also observable in

tumours of the bone-marrow. Bence-Jones's albumose is occasionally found in cases of sarcoma, hypernephroma, and sometimes in leucocythaemia. In fact he lays great stress, as a symptom, on the extremely rapid loss of weight caused by myeloma, and asserts that more than ever must röntgenography be relied upon, as it reveals early bone changes, and in the case of myeloma shows a very distinct and clear-cut picture. F. E. R.

Dubreuil, L. Les hommes sans cou. Syndrome de Klippel-Feil. [**The neckless man. The Klippel-Feil syndrome.**] *Presse méd.*, 1921, May 4, 353. (*J. de radiol. et d'électrol.*, 1921, **5**, 424.)

From the anatomical point of view, the principal characteristic of the Klippel-Feil (1912) syndrome, is the absence of individualized cervical vertebrae, which are replaced by an osseous mass capable of involving the whole cervical region or only its upper part. In certain cases the upper parts of the dorsal spine are included in the lesion. It is difficult to differentiate between the different vertebrae in this osseous mass. The atlas and axis, very reduced, are even sometimes impossible to discern.

The second characteristic of this syndrome is the presence of a long, wide triangular orifice at the back of the spine, constituting a veritable spina bifida.

The thorax reaches up to the base of the skull, forming a sort of 'cervical thorax', justifying the appellation of 'men with no neck' given to persons suffering from this malformation. The head, in fact, seems to rest directly upon the trunk, and, being buried between the shoulders, its movements are extremely limited, and the hair grows very low, below the bi-acromial line.

To these signs are added other characteristics (such as scoliosis and kypho-scoliosis, round back) which have given rise to errors of diagnosis because of the resemblance to sub-occipital Pott's disease. Radiography reveals immediately the arrangement of the cervical vertebrae and enables an exact diagnosis to be made in doubtful cases. S. U. L.-B.

Radiotherapy

Jüngling, O. Zur Behandlung des Sarkoms mit Röntgenstrahlen. [**B.**] [**On the treatment of sarcomata by X-rays.**] *Strahlentherapie*, 1921, **12**, 178.

In reviewing the results of the X-ray treatment of sarcomata it is somewhat difficult to compare results obtained by modern technique with those obtained 15–20 years ago. The author has adopted for this purpose the grouping suggested by Kienböck :

(*a*) Sarcomata which completely disappeared ;
(*b*) those which definitely decreased in size ;
(*c*) those where no alteration could be demonstrated.

He considers these divisions more useful than the grouping adopted by Seitz and Wintz, which is based upon the original clinical findings in each case. The latter method gives a partial answer to the question of what can be done with inoperable, isolated tumours, but is of no assistance in answering what is, after all, the point of greatest surgical interest—namely, which sarcomata should be submitted to operation and in which operable cases

treatment by radiation is permissible. The following statistics are compared: Kienböck's, 90 cases, covering the period 1902–5, the period of slight or no filtration. Müller's, 35 cases, 1912, the period of aluminium filtration. The Tübingen Clinic, 47 cases, covering the period 1917–20, the period of heavy filtration. Seitz and Wintz, 70 cases, 1919.

Kienböck	Tumours disappeared 17·8 %	decreased in size 57·8 %	unchanged 24·4 %
Müller	,, ,, 31·4 %	,, ,, 45·7 %	,, 22·8 %
Tübingen Clinic	,, ,, 31·9 %	,, ,, 44·7 %	,, 23·4 %
Seitz and Wintz	,, ,, 31·4 %	,, ,, 48·6 %	,, 20·0 %

The conclusions drawn are:

(1) The modern method of heavy filtration has not produced any notable improvement upon the results obtained with aluminium filtration.

(2) Whereas formerly (1902–6) one patient in every five was apparently cured, the figures now are one in three; yet during the last three years 46 per cent. of such patients died.

(3) The percentage of sarcomata proving refractory to radiation has remained almost unaltered. This is to be attributed less to an insufficient technique than to some quality inherent in certain sarcomata—every fourth or fifth sarcoma falls into this category.

(4) The statement made by Seitz and Wintz that 60–70 per cent. of the erythema dose is lethal for sarcomata requires the strictest investigation, for, if true, the whole problem would be solved, since there is practically no part of the body which cannot be given this dose with modern instrumentation and technique. As, however, some 20 per cent. of sarcomata still prove entirely refractory, a definite lethal dose cannot yet have been found.

The question of dosage is discussed at some length, and the author comes to the conclusion that for sarcomata in general the establishment of an average lethal dose is not of practical value. Different types of tumour respond at different rates to radiation, e.g. a lymphosarcoma is more sensitive to X-rays than a round-celled sarcoma. Also, as with the skin, there is a relationship between the latent period and the degree of reaction produced—the shorter the latent period the stronger the reaction. As a general rule the disappearance of a sarcomatous tumour should be obtained by degrees and a reasonable time given to the process—it is a mistake to burden the organism by producing too rapid an absorption of a large tumour. Immediate destruction of a tumour should be attempted only when by pressure it threatens life.

(5) As to the choice of treatment it is not at present practicable to foretell which tumours will respond to radiation or prove refractory. The results of radiation of different types of tumour is discussed. Lymphosarcomata generally respond well and should preferably be treated by radiation. Osteosarcomata give varying results. Generally speaking, where operation gives good results, as in myeloid tumours, preference should be given to surgical measures; where, however, these do not give such satisfactory results—as in periosteal tumours—and entail severe operation, radiation should be given a trial first. A summary of 47 cases and a bibliography is appended. E. M. W.

Béclère, A. Sur la Rœntgenthérapie des fibro-myomes utérins d'après trois cents nouvelles observations. [**The X-ray therapy of uterine fibro-myomata after three hundred new observations.**] *J. de radiol. et d'électrol.*, 1921, **5**, 449.

In the *Journal de Radiologie et d'Électrologie*, July–August 1919, the author described his observations on 400 cases, and the present paper is a continuation of that work. The two questions discussed are the clinical aspect and the question of technique, and the author applies himself chiefly to the former.

I. Clinical observations. A. **Condition of the patients before treatment.** (a) *Age.* The ages varied from under 30 years to over 50 years, 67·66 per cent. being between 40 and 49 years. (b) *Dimensions of uterine tumours.* These were grouped into two classes: (i) intrapelvic, 8 per cent.; (ii) developing into the abdominal cavity, 92 per cent. The method of measuring the size of the tumours is described. (c) *Functional troubles due to the uterine tumours.* In most cases metrorrhagia was the predominant symptom, often leading to profound anaemia; other symptoms for which treatment was sought are given. (d) *Concomitant or preceding affections.* These are very numerous. B. **Results of treatment.** The two chief results were, a disappearance of the metrorrhagia with cessation of menstruation in 294 cases and a decrease in size of the tumour in all cases. (a) *Number of menstrual periods before the menopause.* In only 3·4 per cent. of cases were there more than three periods. (b) *Decrease in the size of the uterine tumour.* In 26·8 per cent. of cases the tumours could not be felt at all by the bi-manual method at the end of the treatment. In the other cases the decrease continued to a greater or less extent after the irradiations ceased. The initial marked decrease in volume is, according to the author, diagnostic of fibro-myomata; if this does not occur, he states, the tumour is not a myoma or not exclusively one. In the most favourable cases the diminution in height is about one centimetre per week. It is independent of the ovarian function. (c) *Errors in diagnosis.* In two cases irradiated the tumours were ovarian although they had all the appearances of uterine fibroids. (d) *Recurrence.* The suppression of the ovarian function is accompanied not only by a cessation of menstruation but also by vasomotor disturbances ('heat flushes'), to which he attaches great importance. The significance of its appearance and disappearance is explained. The percentage of recurrence was 3·4 per cent., and these were all dealt with by repeating the treatment. (e) *Failures.* Only those cases should be considered as failures in which, while there was no other lesion of the generative organs, the patient was not cured. On these lines the author's failures were 1 per cent., these are described. (f) *Complications.* Under this heading are included polypi, carcinoma of the uterine mucosa, and ovarian cysts: these can all be present with a fibroid without recognition. During treatment submucous fibroids may be extruded as polypi; this occurred in 1·33 per cent. of cases. Carcinoma of the uterine mucosa is the most serious but most rare complication: two cases of this are described, also two cases of ovarian cysts which, sooner or later, called for treatment. (g) *Dangers and unpleasantnesses of treatment.* The only danger is acute X-ray dermatitis and can easily be avoided; the only unpleasantness is a general feeling of malaise with nausea either on the same day or the day after the irradiation. (h) *Sequelae of treatment.* As regards symptoms at the menopause the author has found no difference between irradiated and non-irradiated cases. The only point

is that after the menopause irradiated cases feel stronger and not so susceptible to fatigue, and the author thinks this may be due to the removal of a focus of infection. C. **Technique of treatment.** A full description of the author's technique since 1908 is given; in recent years more intense and penetrating rays with increased screening have been used. This is followed by a description of the apparatus used and the dose.

II. Indications and contra-indications for X-ray therapy. These are discussed at some length under three headings: (1) general indications for curative treatment; (2) contra-indications for surgical treatment; (3) contra-indications for X-ray therapy, and the conclusions arrived at are that suppuration or gangrene of the tumour alone demand surgical intervention, and that X-ray therapy is only contra-indicated when an emergency operation is needed.

III. Method of action and of using X-rays. The French and German methods are contrasted; by the former the tumour is attacked by the rays direct, and by the latter the ovaries are attacked and destroyed, causing regression of the tumour through the resulting menopause. According to the author, one of the great advantages of the French method is that the doses at the various séances are not so large, and that therefore there are no after-effects, or at most these are very slight and not severe enough to interfere with the patient's normal mode of living.

IV. Comparison between X-ray therapy and radium therapy. The author considers that the X-rays are preferable in the case of fibroids because of their size, and would use radium for more limited lesions such as carcinoma of the body of the uterus. Radium may cause an old salpingitis to light up again, whereas X-rays, it is claimed, would benefit such a condition by suppressing the menstrual congestion. The disadvantages and unpleasantnesses caused by radium are contrasted with those caused by X-rays.

In conclusion, the author states that in the treatment of uterine fibroids, except under special conditions which necessitate instant operation, X-ray therapy is the treatment of choice; it is the only one which applies to nearly every case and nearly always results in a cure without danger, pain, or alteration in the usual mode of life. P. L.-B.

Schmid, R. Die Strahlentherapie der Myome und hämorrhagischen Metropathien seit dem Jahre 1914. Ein Sammelreferat. [**The ray-therapy of myoma and haemorrhagic metropathies since 1914.**] *Strahlentherapie*, 1921, **13**, 204–71.

This synopsis, with forty-five reports from a large number of public and private clinics on the X-ray treatment of myomata, &c., must be consulted in the original by those interested, as it so exhaustively deals with all the details of the subject as to indications, technique, and results. A similar article on radium treatment will appear in due course. J. H. D. W.

Radium Therapy

Heyerdahl, S. A. **Radium treatment of changes in the thyroid gland.** *Acta Radiol.*, 1921, **1**, 207.

Various authors are referred to who have used radium in preference to X-rays in treating thyroid lesions. Aitkins, of Toronto, is quoted as saying

that in acute cases radium must be supplemented by rest in bed, diet, and drugs. Gamma rays alone are used. Aitkins's technique and the opinions of Claquett, of Chicago, are mentioned. The results of treating eight cases of plain goitre are given; in all the goitre was diminished and there was a change for the better. The inconveniences of the treatment and the danger of telangiectasis are dealt with. The author's opinion is that for this type of case radium will only be used when operation is out of the question. The technique is described. Eight cases of toxic goitre were treated, and the results and the effect of the treatment on symptoms is described. Detailed notes of eight of the sixteen above-mentioned cases are given and followed by those of four out of eight cases of struma malignum, of which five showed temporary improvement and three no improvement. P. L.-B.

Kurtzahn, H. Über den Anwendungsbereich und die Anwendungsweise des Radiums bei inoperablen malignen Tumoren. [**On the sphere and method of application of radium in malignant tumours.**] *Strahlentherapie*, 1921, **13**, 72–87.

The value and limitations of radium and of X-ray treatment in differing sites of inoperable malignancy are sketched, and the methods employed by the author with 100 mgm. of radium element in four 25-mgm. tubes are given, biological dosage being made on the skin of a dog, and the erythema and 'ulceration dose' being found for varying combinations of the tubes and times of application. 1 mm. brass is recommended as the best filter, or 0·5 brass where beta effect is also required. In rectal cases 100 mgm. for 2–4 hours is combined with deep X-ray therapy, which is also used in bladder and prostatic cases with 50 mgm. (up to four hours). Mouth and oesophageal technique is also given: for the latter a gastrostomy is always first performed, and a silk thread swallowed, to which the radium tubes are attached, and drawn down into the stricture, after its site has been fixed by sounding and X-ray examination. 100 mgm. with 0·5 and 1 mm. lightly nickelled-brass filters are left in position for not over six hours. One case improved so much that against advice he had his gastrostomy closed.

J. H. D. W.

Radiobiology

Wood, F. C., and **Prime, F.** **Further studies in radiation dosage.** *J. Cancer Research*, 1921, **6**, 177.

Dr. Wood showed a series of lantern slides at the meeting of the American Association for Cancer Research on March 24, 1921, by which the fact was illustrated that, contrary to statements emanating from Germany, there is no destructive carcinoma or sarcoma dose; that is, no fixed amount of X-ray can be assumed to destroy the cells of any one tumour, for apparently the dosage differs greatly both in man and animals for the same microscopic type of tumour. As was shown by charts in animal tumours the required dosage is from two to eight erythema doses, and the sarcomata vary in resistance as well as the carcinomata. One interesting point is the greatly delayed appearance of tumours in regions where the cells received a sublethal dose. In a mouse tumour, which ordinarily appears within

a week and gains a fair size in two weeks, the appearance may be delayed for a month or more and the tumour grow very slowly afterwards. If a transplantation be made from this tumour into another animal the growth-rate will rapidly approximate normal. The authors suggested that, since two or three months in a mouse's life are equivalent to the same number of years in the human being, it is possible that late recurrences (three, four, or five years after the symptomatic cure of malignant tumours in man) may be seen when such symptomatic cure has been obtained by either radium or X-rays. Most of the experiments were made by raying the tumour particles *in vitro* and then transplanting them; if the tumour is rayed in the mouse the animal is killed in a few days by the radiation. If the tumour be immediately transplanted it grows in the new host unless it has been given a lethal dose. This lethal dose is approximately 10–20 per cent. more than when the cells are exposed *in vitro*.

In the subsequent discussion Wood stated that he had not found any increase in the destructive action of rays given off by tubes running at 180,000 volts as compared with those running at 120,000 volts, measuring peak voltages between 12·5 cm. spheres. In all his tests there had been no question of absorption or of scattered radiation, the tumour having been exposed directly to the rays. The advantage of the high voltage machines lay in the greater penetration which could be obtained, but he saw no reason to assume that they would be any more effective on superficial growths for equal X-ray dosage. In reply to another inquiry he said that he had not noticed any increase in growth-rate of the tumours unless very small doses were given; and that tumours which had been greatly slowed at their first transplantation, grew at their regular rate in the second transplantation. Asked as to the exact mechanism of the effect of X-rays on the cell and whether the connective tissue does not play an important part in destruction of the tumour cell, he said that all that was known is that the division mechanism is interfered with, cells in a resting stage being much more resistant to radiation than those in mitosis. Experience with animals showed that it takes very large doses to kill all the cells in a tumour; those in the centre of the growth are killed partially by direct action and partially by the thrombosis which occurs early in the smaller capillaries. The periphery of the tumour, however, is, as a rule, better nourished, and there the cells require maximum dosage. He had not observed that connective tissue is capable of destroying cancer cells, though such cells might be enclosed in dense scar-tissue and remain quiescent for a considerable period. But there was a possibility that they might again begin to grow years after their inclusion, as had frequently been observed in human cases in the late recurrences in operation scars. In response to a further inquiry as to the method adopted, Dr. Wood said that this was 120,000 volts, peak, measured between 12·5 cm. spheres. The tumour fragments used *in vitro* were 1–2 mm. in diameter. If whole tumours be used, or if the tumour be irradiated in the mouse, the superficial layers nearest the tube will be killed, while the deeper layers will not. At this voltage 10 cm. of tissue absorbed 50 per cent. of X-ray incident on the surface; this 50 per cent. including not only directly transmitted rays, but also scattered ones. His own experiments had all been devised to avoid the complications brought into the problem by scattering and absorption.

Duane thought that the difference between the dosage measured by Wood and that reported from Germany might be due to scattering.

According to recent reports, at a distance of 10 cm. below the skin scattering may increase the dosage $2\frac{1}{2}$ times. He suggested that if the pieces of tumour in human cases were surrounded by bits of tissue they might, perhaps, receive $2\frac{1}{2}$ times as much radiation as they did under Wood's experimental conditions. W. S. L.-B.

Hausser, K. W., und **Vahle, W.** Die Abhängigkeit des Lichterythems und der Pigmentbildung von der Schwingungszahl (Wellenlänge) der erregenden Strahlung. [**The dependence of light-erythema and pigment-formation on the vibration number (wave-length) of the exciting ray.**] *Strahlentherapie*, 1921, **13**, 41–71.

Discusses the physical problems of electro-magnetic waves, pointing out the incorrect use of the terms 'chemical rays' for the ultra-violet (chlorophyll being most influenced by red wave-lengths) and 'heat-rays' for the infra-red (the sun's maximum (600 $\mu\mu$) being within the visible spectrum), and describing the method used for experimental homogeneous radiation with differing wave-lengths of equivalent intensity, on the dorsal aspect of the forearm. The maximum effect was found in the region well beyond the visible spectrum (800–400 $\mu\mu$), and in a narrow range between 320 and 280 $\mu\mu$, with a sharp peak just under 300 $\mu\mu$. The bearings of this on sun- and mountain-cures and on quartz-light treatment are discussed, and the advantages of a biological method of dosimetry against a direct physical, or physical plus a filter, or photophysical or chemical, are advanced, with particular application to the heliotherapy of lung-tuberculosis, and the uselessness of the treatment of laryngeal tuberculosis with light reflected from *glass* mirrors (special ones should be used) is contrasted with the value of the Finsen light in lupus. J. H. D. W.

Zwaardemaker, H., et **Feenstra, T. P.** Substitution du potassium par l'émanation de radium dans le liquide de Sydney Ringer. [**Substitution of potassium in Ringer's fluid by radium emanation.**] *Compt. rend. Soc. de biol.*, 1921, Feb. 26. (*J. d. radiol. et d'électrol.*, 1921, **5**, 430.)

Zwaardemaker, H. Le paradoxe radio-physiologique. [**The radio-physiological paradox.**] *Compt. rend. Soc. de biol.*, 1921, April 23. (*J. de radiol. et d'électrol.*, 1921, **5**, 430.)

After having shown that the potassium in the Ringer's fluid can be replaced by any radio-active atom, the authors agree as to the necessity for intervention of the radio-active element alone, and not of chemical or ionic action.

The author of the second communication thinks it possible to affirm that alpha and beta rays have, on the hearts of the frog and of the eel, antagonistic actions, which he attributes to the action of changes of opposite sign borne by these radiations upon sensitive cells. S. U. L.-B.

MEDICAL SCIENCE

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	SIDNEY RUSS, D.Sc.
Biochemistry . . .	C. G. L. WOLF, M.D.

All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

ACUTE RHEUMATISM AND RHEUMATOID AFFECTIONS

Aetiology. Fedeli alludes to Grenet's article (vide *Medical Science*, 1920, **3**, 3) and records another example of the contagiousness of acute rheumatism. He was recently called to see a boy, aged 13, who was suffering from a typical attack of acute articular rheumatism. A few days later the patient's brother, who was sleeping in the same bed, developed the disease, and shortly afterwards another child and a woman, who had been staying in the same room, were similarly attacked. The father of the first two children was a rheumatic subject, but in the last two cases there was no hereditary history of rheumatism.

At the Section on Practice of Medicine of the American Medical Association, in April 1920, St. Lawrence reported on 85 children admitted to the children's cardiac clinic at St. Luke's Hospital, New York, each of whom had presented one or more rheumatic manifestations before the tonsils were completely removed. The tonsils were much hypertrophied in 13 per cent., moderately hypertrophied in 69 per cent., and not enlarged in 18 per cent. In 73 per cent. they were the site of recurrent inflammation before tonsillectomy. One or more attacks of acute rheumatic fever had occurred in 42 cases before the tonsils were removed. After tonsillectomy there was no recurrence in 35 cases, or 84 per cent. Sixty-one cases showed myositis and pains in the bones or joints before operation, and there was no recurrence in 47 cases, or in 77 per cent. St. Lawrence concludes that tonsillectomy is the most important measure at present available for the prevention of acute rheumatic fever and the allied rheumatic manifestations.

In the subsequent discussion Lambert stated that though in persons of all ages teeth were more often the cause of rheumatic fever than tonsils, in children the tonsils predominated over the teeth in their liability to cause infection.

Epidemiology. According to Riesman, the death-rate in Philadelphia for acute articular rheumatism, including rheumatic fever, was 83 in 1916, 111 in 1917, 64 in 1918, 78 in 1919, and 104 in 1920, or from 3·59 to 6·33 per hundred thousand. The greatest mortality from articular rheumatism was in the age period from 5 to 15.

Symptomatology. The following *rare forms of muscular and articular rheumatism* are described by Janowski, of Warsaw: (1) Rheumatism of the thoracic muscles, often diagnosed as pleurisy. Janowski maintains that the absence of a rub and of a cough in such cases should lead the doctor to make a careful palpation of the skin, bones, and intercostal spaces of the lower end of the thorax. A localized sensitiveness of the intercostal

muscles is then found and is very pronounced in febrile cases. (2) Rheumatic affection of the sacro-iliac synarthrosis, which is very rare. According to the writers quoted in Pribram's monograph, cases in which this joint is involved as well as others amount to only 0·2 to 0·7 per cent. of all cases of articular rheumatism. Exclusive localization of rheumatism in this joint is so extremely rare that no statistics are available. Janowski, however, has seen a few cases of this kind and has found that rheumatic affections of the sacro-iliac joints were decidedly more frequent during the recent war than previously. The condition is very liable to be mistaken for sciatica. (3) Rheumatism of the intervertebral joints. Janowski has seen a case of rheumatism affecting the four cervical vertebrae from the second to the fifth. The symptoms were so severe that the condition might have been mistaken for basal meningitis, had not the rapid action of salicylates justified the diagnosis of a rheumatic process. He has also seen cases of rheumatic affection of the dorsal intervertebral joints, in which the disease has a subacute course, resembling in some respects Pott's disease or syphilis of the vertebral column. (4) Rheumatism of the costo-vertebral articulations, the four or five lower ribs usually being involved. If the affection is accompanied by a rise of temperature it is sometimes diagnosed as pleurisy or may be mistaken for pyelitis or paranephritis. Owing to its apyrexial course, intercostal neuralgia and atypical attacks of cholelithiasis can be excluded. In all cases of this kind the diagnosis is established by the remarkable effect of salicylates internally and externally.

Bittorf, of the Breslau University Medical Policlinic, remarks that as compared with the typical joint affections other localizations of acute rheumatism are very uncommon, *acute rheumatic periostitis* being one of the greatest rarities. He records two examples of this condition in vigorous men, aged 20, who came under treatment as cases of typical acute articular rheumatism. In one case both thighs and in the other one thigh, were thickened, swollen, and tender in the middle third, the overlying skin being slightly reddened. Osteomyelitis could be excluded in each case. The condition subsided with rest in bed, warm compresses, and large doses of salicylates.

Popper, of New York, records a case of *acute articular rheumatism following acute otitis media* in a boy aged 9 years. He was treated by salicylates, and in less than 24 hours there was a decided relief of all the symptoms with a marked improvement of the general condition. The case was quite distinct from the bacteriaemic condition simulating rheumatism which not uncommonly follows acute otitis media.

A case of acute articular rheumatism complicated by *appendicitis* and rapidly cured by intravenous injection of perchloride of mercury is reported by Bindi (1).

Herbert divides the heterogeneous medley of diseases generally classed under the heading of 'rheumatic' or 'gouty' into two groups, according as the temporo-maxillary joint is or is not involved. He maintains that in gout or true rheumatism the *jaw-neck syndrome*, i. e. involvement of the temporo-maxillary and occipito-atlantoid or upper cervical intervertebral joints, is always absent, and conversely that in the toxic and infective group, in which the underlying cause is gonorrhoea, rheumatoid arthritis, dysentery, oral sepsis, &c., it is practically always present.

Schmidt, of Bad Pistyan, gives an account of a *bilateral disease of both hip-joints* which has not hitherto been described. During the first years of the disease the patient usually complains of pain in one hip, which is

more or less painful and used with difficulty. Examination of the supposedly healthy hip on the opposite side frequently shows some limitation of movement in spite of the absence of any subjective symptoms, the patient being very surprised to hear that both hips are affected. It is not till a later stage that subjective symptoms also appear on the other side. Finally, movement in any direction becomes extremely limited on both sides. Sitting down or standing up is only possible with assistance, and at night lying in a definite position is as painful as a change of posture. When there is only a slight limitation of movement the X-ray picture may be negative, but at a later stage bilateral exostoses are seen, though areas of atrophy are absent. The aetiology of the condition is not yet clear. The disease develops simultaneously on both sides, and early recognition of the bilateral affection is important not only from a diagnostic and prognostic standpoint, but also for purposes of treatment. The use of baths, massage, and gymnastics not only prevents the condition getting worse, but also causes considerable relief.

Schittenhelm, of Kiel, who has recently seen three examples in civil life, alludes to the affection described by Schlecht and himself in soldiers under the name of *polyarthritis enterica* or *pseudo-rheumatica* (vide *Medical Supplement*, 1918, **1**, 295). The description, which was based on a large number of observations made on active service, showed that the condition, which was a well-defined one, might occur not only after well-marked dysentery but also after quite mild intestinal catarrh and even in persons who had no intestinal catarrh at all. It was a joint affection which had a well-marked polyarticular character accompanied by a serous effusion. It usually ran a subacute course, not infrequently lasted several months, and almost invariably ended in recovery. Transformation into arthritis deformans or suppuration was never observed. The frequent occurrence of eye disease, especially conjunctivitis, which was found in 29 per cent. of the cases, was characteristic, as well as combination with non-specific urethritis, which was present in 2·5 per cent. The condition differed from acute articular rheumatism in its subacute onset, obstinate protracted course, intense exudation but slight degree of inflammation, absence of heart complications, rarity of sweating, involvement of the eyes and urethra, and lastly little or no reaction to salicylates. The condition resembled that described in 1916 by Reiter who found spirochaetes in the blood removed by venepuncture (vide *Medical Supplement*, 1918, **1**, 214). As a rule, however, bacteriological examination of the blood and joint fluid was quite negative. Schittenhelm and Schlect regarded the intestine as the portal of entry of infection, even when no definite intestinal disease was present.

Stühmer, of the Freiburg University Skin Clinic, reports four cases of Reiter's 'spirochaetosis arthritica', in which, with one exception in which the joints were not affected, involvement of the joints was associated with conjunctivitis and non-specific urethritis. Repeated examination of the secretions, blood, puncture fluid, and even an excised portion of the conjunctiva failed to show any spirochaetes, and only in the urethral pus were Gram-positive bacilli sometimes found. Stühmer therefore concludes that there is no justification for the term 'spirochaetosis arthritica' to describe this condition.

Petrén's paper on *arthritis deformans and other forms of chronic rheumatic diseases of the joints* deals with three joints, the hip, shoulder,

and knee, and he describes methods of examining the hip and shoulder which he has found more accurate than those in common use. In the examination of the hip he attaches great importance to finding out the very widest range of movement of which the joint is capable. Testing the range of flexion, he does not content himself with a range of 90°, and he has obtained a range of up to 150° in several cases. To test the degree of rotation, he places the patient on his back, flexing the limb at hip and knee to about 90°. The range of rotation at the hip can now be estimated with considerable accuracy. He also tests the range of abduction while the patient is on his back; with good mobility the limb may be brought almost to the horizontal plane. Both rotation and abduction being tested while the limb is flexed at the hip, wider ranges of movement are obtained than with the limb extended at the hip. Testing the mobility of the shoulder-joint, he describes a method 'far superior' to that in ordinary use. The arm is abducted to 90° so that the upper arm is horizontal. Rotation about the shoulder-joint is now performed with the elbow flexed to 90°. Thus the position of the forearm clearly shows the degree of rotation about the shoulder-joint. Under normal conditions the range of rotation is about 180°, so that the forearm can be brought from the vertical position, pointing downwards to the other vertical position, pointing upwards. In chronic rheumatic disease of the shoulder-joint this normal rotation of 180° is reduced to 90° or less.

A study of 103 cases of arthritis deformans limited to the hip and observed at Petrén's hospital between 1910 and 1920 brought out the following points. The term malum coxae senile is misleading; in 8 per cent. the disease developed before the age of 40, in 37 per cent. before the age of 50, and in 68 per cent. before the age of 60. Only in 13 per cent. did it develop after the age of 65. In the overwhelming majority of cases the disease was bilateral, and as the unilateral cases were of comparatively recent standing, doubt is expressed as to the very existence of unilateral disease in a case which has lasted for many years. In his discussion of various methods of treatment, Petrén gives first place to passive movements; heat, salicylates by the mouth, and massage are recommended, but only as of secondary importance. The results achieved by passive movements were often excellent, judged by functional standards. Judged by X-ray standards, the results were not impressive, and the conclusion drawn is that the improvement effected is due to the pain and rigidity of muscular spasm being overcome by treatment which has little effect on the bony changes. An exercise recommended for arthritis of the shoulder-joint is hanging by the hands—a manœuvre which brings the arms into a vertical position, pointing upwards.

Treatment. Lutembacher remarks that in spite of our possessing an active specific remedy in salicylate of soda, relapses of acute articular rheumatism are remarkably frequent. He attributes this occurrence to inadequate duration of the treatment. He therefore recommends that large doses of the drug should be continued for fifteen to twenty days after the temperature has fallen, in the absence of signs of intolerance, even if the arthritis has entirely disappeared. If the dose has to be reduced or the drug has to be suspended entirely for a time, the large doses should subsequently be resumed for three or four weeks. During the following weeks doses of 3 to 4 gm. daily are given. The treatment is continued systematically for 12–18 months after the attack, 2–3 gm. of sodium

salicylate being given daily for 10 days, either by mouth or intravenous injection, in spite of the absence of any recurrence. Lutembacher has treated eight cases by intravenous injection of sodium salicylate in doses of 3 gm. daily, associated with oral administration of the drug by night.

Gilbert, Coury, and Bénard, who have employed intravenous injections of sodium salicylate in the treatment of acute articular rheumatism during the last two years, have come to the conclusion that this method should not be substituted for the ordinary mode of administration even in cases of gastric intolerance, but should be reserved for severe cases with endocardial or cerebral complications.

In cases of gastric or nervous intolerance Colombo recommends hypodermic injection of sodium salicylate in the neighbourhood of the affected joint or joints. The first injection consists of 2 c.cm. of a 3 per cent. solution of sodium salicylate, the following day 2 or 3 c.cm. of a 5 per cent. solution are given, and the same doses are repeated for six or seven days or more. Colombo regards it as advisable to continue the injections for three or four days after disappearance of all the symptoms. He has found that this method shortens the duration of the disease, prevents its spreading to other joints, does away with the discomfort caused by intolerance of sodium salicylate, and arrests the development of the several complications of acute articular rheumatism.

Local injections of aspirin, phenacetin, or antipyrin are also recommended by Lampronti. He found that 4–6 c.cm. of a saturated solution of aspirin or phenacetin gave prompt relief, but that in 6–7 hours, or a little later, the pain returned with almost the same intensity. On the other hand, injection of a 3 per cent. solution of antipyrin in doses of 8 c.cm. in the neighbourhood of the affected joints was followed by prompt and permanent cure after a few days' treatment (vide also *Medical Science*, 1920, **3**, 6).

Hanzlik and Scott, with the collaboration of Weidenthal and Fetterman, of Cleveland, made comparative studies of the therapeutic efficiency, toxicity, and effects on renal function of cinchophen, neocinchophen, and novaspirin, which had been advertised as superior substitutes for salicylates in the treatment of rheumatic fever. Their results were as follows: (1) Cinchophen gave partial relief in doses of from 3–6 gm., while neocinchophen required a somewhat higher dosage, viz. 3 to 8 gm. for partial, and from 11 to 16 gm. for complete relief. (2) Novaspirin was therapeutically worthless, not giving even partial relief, this being due to inadequate concentration of salicyl in the tissues. (3) Large doses of cinchophen and neocinchophen, such as are necessary in the treatment of rheumatic fever, produced characteristic symptoms of salicylism, which were, however, less pronounced than those caused by corresponding doses of salicylates. Cinchophen differs from salicylates in causing epigastric pain, owing presumably to local irritation by the drug. (4) Large doses of cinchophen in both febrile and afebrile individuals and of neocinchophen in febrile patients produced a depressant action on the circulation, shown by slowing of the pulse-rate. (5) Cinchophen is injurious to the kidney, as indicated by the occurrence of albumin and sometimes casts and white blood corpuscles and a diminution in the excretion of phenolsulphonephthalein. Albuminuria and a diminution in the excretion of phenolsulphonephthalein occurred in about half the cases to which neocinchophen had been given. (6) As compared with salicylates cinchophen appeared to be about equally efficient, while neocinchophen was somewhat less efficient as judged by the

dose necessary for therapeutic relief in rheumatic fever. The toxic symptoms were about the same, and renal injury somewhat less after cinchophen, and both the toxicity and the renal injury are less pronounced than after salicylates in corresponding doses.

In a subsequent paper Chace, Myers, and Killian, of New York, record their observations on the same subject, their conclusions being as follows: (1) The salicylates and cinchophen group of drugs show comparatively little difference in their analgesic, antipyretic, and 'uric acid eliminating' effects. (2) There appears to be no relation between the therapeutic efficiency of these drugs in infectious arthritis and their influence on the blood uric acid. (3) In the series of cases reported by the writers cinchophen and neocinchophen seemed to have a more specific effect in the cases of severe arthritis. (4) The salicylates have the distinct disadvantage of producing marked proteinuria and casts when given in large doses. Cinchophen and neocinchophen are therefore the drugs of choice when for any reason it seems desirable to favour the kidneys. Moreover, the latter drugs appear to produce their therapeutic effect in smaller doses. (5) The salicylates have the advantage of being better assimilated by the rectum. (6) Cinchophen and neocinchophen, especially when given with alkalis, are better tolerated by the stomach than salicylates. (7) Although a few cases of marked idiosyncrasy to the salicylates have been reported in the nature of an allergic reaction, the writers' experience is that patients are more liable to have vasomotor disturbances of the urticarial type from cinchophen, but no serious examples of the latter were observed.

Fantoni has treated more than a hundred cases of acute articular rheumatism by intravenous injection of perchloride of mercury. The treatment consisted in injection of 4 mgm. of perchloride in 4 c.cm. of normal saline daily for four days in succession. No symptoms of intoxication or intolerance were observed, and a cure was usually obtained after seven injections. The most rapid effects were observed in the acutest cases with high temperature and severe joint manifestations, especially patients in their first attack. In such cases the symptoms often disappeared after four or five injections. The results were less rapid in the subacute and relapsing forms. The advantage of perchloride of mercury over salicyl preparations is that in the doses given it is always well borne, and, unlike salicylates, does not depress the heart or irritate the digestive tract or kidneys. The only contra-indication to its use is an intercurrent nephritis.

Cases of acute articular rheumatism successfully treated by intravenous injections of perchloride are also reported by Bindi (1), (2).

Viola records nine cases of acute articular rheumatism in soldiers treated by intravenous injection of colloidal sulphur. As a rule he did not give more than three injections, each consisting of 1 c.cm. either daily or every other day. The rationale of the treatment consisted first in its causing a polymorphonuclear leucocytosis, which is the best method of defence of the organism against bacterial invasion, and secondly, in supplementing the deficiency of sulphur in the affected joints (Maillard and Bourges). The results obtained when the injections were given early were as follows: (1) disappearance of pain, fever, and swelling within a few hours; (2) considerable shortening of the duration of the disease; (3) prevention of visceral complications. On the other hand, the injections were of little avail in advanced and complicated cases. The general reaction in Viola's cases following the injections was negligible. These results do not

agree with those of some writers, especially A. Robin, who attribute the value of colloidal metals to the reaction which they produce, but harmonize with those of Maillard as to the re-establishment of the sulphur deficit.

Meyer-Bisch, of the Göttingen University Medical Clinic, records fourteen cases of chronic joint disease treated by intragluteal injections of sulphur, and comes to the conclusion that in a surprisingly large number of cases of severe and obstinate joint disease a considerable improvement is produced by the treatment, amounting, in some cases, to disappearance of the symptoms. His cases were divided into three groups: (1) primary chronic arthritis and osteo-arthritis deformans; (2) chronic or acute rheumatic polyarthritis; (3) chronic rigidity of the vertebral column (Bechterew's disease). The treatment consisted in intragluteal injection of 1 gm. of sulphur in 100 gm. of olive oil at intervals of six to seven days in doses of 2 c.cm., which were gradually increased to 5 c.cm. and 10 c.cm. In primary chronic polyarthritis and chronic rheumatic polyarthritis there were practically no failures. Less striking but distinct improvement was obtained in chronic rigidity of the vertebral column. Cases of osteo-arthritis deformans chiefly localized in the large joints were not suited for the treatment. Lastly, sulphur could not be regarded as a substitute for salicylates in acute polyarthritis. Molnár, assistant at the Buda Pesth University Second Medical Clinic, also found intragluteal injections of sulphur emulsion of value in chronic poly-arthritis deformans and acute polyarthritis, though it was unable to prevent the development of endocarditis.

Snyder and Ramirez, of New York, during the last four years have treated about seventy cases of chronic arthritis with intravenous injection of foreign protein. Both typhoid vaccine and secondary proteose were used, the doses being ten million typhoid bacilli or from ½ to 1 grain of secondary proteose prepared from milk. The patients experienced less nausea, head-ache, and weakness after the use of secondary proteose than after injection of typhoid vaccine, so that patients who had been treated by both typhoid vaccine and proteose much preferred the proteose for subsequent injections. Both preparations appeared to be equally efficacious in relieving the pain and improving the motion in the joints. Cases of chronic arthritis which had not been relieved by routine treatment consisting of sodium salicylate, aceto-salicylic acid, colchicin, cinchophen, hot packs, bathing, or massage were, as a rule, materially benefited by intravenous administration of small doses of foreign protein.

Draper, of New York, remarks that though the mode of action of the bee-sting in chronic arthritis is at present comparatively obscure, the effect upon the blood count, the skin reactions, the reports of generalized oedema, and the rise of temperature suggest acute protein shock analogous to the effects obtained by injections of many foreign proteins. The family and personal history which arthritic patients give of urticaria, angio-neurotic oedema (bee-sting effects), and asthma, and, in addition, the well-known feature of joint involvement seen in serum disease, seem to indicate that there is a relationship between this group of phenomena and chronic arthritis.

Pemberton, of Philadelphia, whose previous studies on arthritis were recently noticed (vide *Medical Science,* 1920, **3**, 4), states that the great majority of chronic arthritics, if placed upon a sharply reduced intake of food or on a starvation basis, will show within a period of one to four days an improvement in their subjective feelings, lessened tension of the soft tissue, and an added freedom of movement. This improvement may occur

even in the presence of causative foci of infection, but treatment based on a reduced caloric intake should never be attempted in the presence of such removable infection. In the early stages following the institution of a sharply reduced diet there may be a rapid loss of weight. Under these circumstances improvement in the arthritis may be very striking owing to the fact that catabolism is running ahead of anabolism. As the plane of basal metabolism falls, however, to a lower level and becomes adjusted there with equilibrium of weight, improvement may be much less obvious, or may even cease entirely.

Wright and Hubbard, of Clifton Springs, New York, have also been using with advantage for the last three years the diets recommended by Pemberton for chronic arthritis, viz. restriction of the carbohydrates while avoiding possible complications of metabolism due to too large amounts of fat.

Rosica alludes to Menzer, who maintains that acute rheumatic polyarthritis is a streptococcal infection arising from the respiratory tract, and has always obtained better results by injection of antistreptococcal serum than by the use of salicylates both as regards complete recovery and the avoidance of relapses. Rosica states that he has also had excellent results from injection of antistreptococcal serum in cases of acute articular rheumatism which were refractory to other treatment.

From December 1910 to November 1920, excluding the last three years of the war, Crowe treated 143 cases of rheumatoid arthritis by vaccines prepared from *Staphylococcus epidermidis albus* (var. *deformans*), which he regards as the primary cause of rheumatoid arthritis. No other treatment was given to any of the successful cases, except simple symptomatic measures, such as aspirin occasionally for the relief of pain, and latterly some mild hydrotherapy. The initial dose in the enormous majority of cases was half a million. The daily weight was found to be a satisfactory method of controlling the dosage. The interval with small doses was three to four days, with larger doses a week. Crowe claims that better results were obtained by the vaccine than by any other method of treatment. Among sixty-two cases, of which the notes were fairly complete, only 21 per cent. failed to respond in some degree, 9·5 per cent. improved but slightly or relapsed early. 70 per cent. were cured for the time being as far as cure was possible, and of them 15, or 25 per cent., still maintained their position at the time of publication of Crowe's paper.

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J. D. R.
C. L.

CEREBROSPINAL FEVER

Aetiology. An outbreak of thirteen cases of cerebrospinal fever which occurred near Edinburgh in July 1918, among a company of 700 recruits, drawn from agricultural districts in the north of Scotland, is described by Miller. All the cases developed after an attack of influenza which acted by lowering the resistance and by mechanical dissemination of epidemic strains of the meningococcus through coughing and sneezing. Another aetiological factor was that all the men were country recruits, who, owing to lack of immunity, are notoriously susceptible to infection of any kind.

Epidemiology. According to Newman, the chief medical officer of the Ministry of Health, the total number of cases notified as cerebrospinal fever in 1920 was 583, and after correction occasioned by dual notification and amended diagnosis was reduced to 559. The number was therefore less by 213 than in 1919, when the amended total was 772. The general incidence, however, is still heavy, compared with that before the war (300 in 1913, vide *Medical Science*, 1920, **3**, 223). In London the greatest number of notifications was received during the last week in April, while outside the Metropolitan area the greatest number of cases occurred a week earlier. The percentage of males among those attacked was 59·9, and of females 40·1 approximately. The mortality was very high, being 70·6 per cent. as compared with 67·2 per cent. in 1919. Of the 395 deaths 53·5 per cent. occurred among children under 10, and of the total number of victims 242 were males and 153 females.

According to De Mello, who describes an epidemic in the Portuguese Indies, little is to be found in medical literature as to the epidemiology and clinical symptoms of cerebrospinal fever in the tropics. De Haan, of Java, claimed to have been the first to have discovered this disease in warm countries in 1908, and about the same time Horn made a study of it on the Gold Coast. Arlo, and Abette and Daniel made two reports to the Société de pathologie exotique on meningitis in French Guinea and in the Belgian Congo in 1916 and 1918 respectively. In India, where it was first noted by Robertson Milne in 1906, it has appeared in various districts, but, as Clemow remarks, it is impossible to say how far the general population is affected. Chalmers and O'Farrel described an epidemic in the Sudan in 1917; one occurred at Madagascar in the same year, and De Mello has recently had private information about cases in Nairobi and Angola. Although practically unknown in the Portuguese Indies, cerebrospinal fever has been observed there since 1904. In the epidemic described by De Mello, which took place in December 1918 in the south of Goa, there were about 500 cases in the

three villages infected. Several were extremely mild and the mortality was below 18 per cent. Children were almost exclusively affected, barely half a dozen adults being attacked. Only one or two cases occurred above the age of 45. There was a larger number of cases below than above six years of age.

Symptomatology. Favrel devotes his Paris thesis to the description of *incomplete forms of cerebrospinal meningitis in the infant* in which the only symptom is bulging of the anterior fontanelle. He recommends that in every infant who presents a distinct bulging of the fontanelle even without fever the possibility of cerebrospinal meningitis should be considered, and lumbar puncture should be performed without delay. Systematic examination of the fontanelle will enable latent cerebrospinal fever to be detected at its onset, thereby causing a reduction of the high mortality and frequency of complications as the result of opportune treatment. The state of the fontanelle should also be studied during the course of the disease before and after lumbar puncture. If the fontanelle subsides after lumbar puncture there is no obstruction. Progressive sinking of the fontanelle in 2 or 3 days under serum treatment appeared to be a good prognostic.

Pestalozza records 10 cases of cerebrospinal fever in infants aged from 18 days to 7 months, observed at the Milan Paediatric Clinic between 1916 and 1920. In three the predominant symptoms were respiratory, and in three gastro-intestinal, while the others presented vague disturbances without definite localization. Seven died, death in one being due to an associated pneumococcal infection of the meninges.

According to Root, who reports a case in an infant aged five weeks, the symptoms of *cerebrospinal fever in the new-born* and in early infancy are usually irregular and obscure. The most important are repeated convulsions, vomiting (not projectile), and, after a week or more, bulging of the fontanelle and rigidity of the neck. Root has found only six other cases on record of meningococcus meningitis in the new-born and early infancy, and in only one of them was there an associated hydrocephalus as in his own cases.

A frequent cause of the failure of specific treatment in cerebrospinal fever, according to Caussade and Remy, is *infection of the cerebral ventricles.* It may be observed at all ages, but it is most interesting in children, in whom it can be detected by definite signs and symptoms, instead of being latent as in the adult, and is more amenable to treatment. A characteristic feature of the hydrocephalic form of cerebrospinal fever in infants is the long duration of the latent stage, the condition being at first mistaken for gastric derangement and respiratory catarrh. The development of hydrocephalus, which is invisible in the adult owing to rigidity of the skull, is shown in the infant by progressive increase in size of the cranium, widening of the fontanelles, separation of the sutures, softening of the skull-bones, depression of the eyeballs, and the development of a rich venous circulation on the scalp. The anterior fontanelle is in a condition of permanent tension, and does not sink down even when fluid is withdrawn by lumbar puncture, and all pulsation in it ceases. The only effectual method of treatment consists in puncture of the ventricles. The injection should be performed into each ventricle alternately every other day. When possible it is advisable to perform cerebrospinal lavage with antimeningococcal serum.

Woringer, of the Strasbourg Faculty of Medicine, reports two cases in infants aged 8 months and 7 weeks respectively, remarkable for the fact that they are the only examples on record of *primary meningococcal infection*

of the ventricles, the meninges of the convexity and spinal cord being unaffected in each case. He attributes the condition to the communication between the ventricles and the subarachnoid space being closed immediately after infection of the ventricles.

According to Nobécourt and Paraf, who record a case in an infant aged 6 months, *cerebral abscess* is a rare complication of cerebrospinal meningitis, only a few cases having been reported by Laignel-Lavastine, Monziols and Loiseleur, Castaigne and Gouraud, Dopter and Westenhoffer respectively. Though liable to be found at various ages, it is most frequent in adults. As in the writers' case, its existence is not suspected during life, and it is not discovered till the autopsy.

According to Charpin, who records an illustrative case, *cranial or spinal meningeal haemorrhage*, with or without ventricular haemorrhage, is a rare complication of cerebrospinal fever in the infant. The clinical diagnosis is usually impossible, and repeated lumbar punctures, and if necessary ventricular punctures, are needed to detect the condition. Complete examination of the fluid obtained by puncture is indispensable in all cases, as the haemorrhages in atypical cases may lead to an erroneous diagnosis. The presence of meningeal haemorrhage in cerebrospinal fever should warrant a very unfavourable prognosis, since no treatment is likely to be efficacious.

Neter, of Mannheim, records a fatal case of cerebrospinal meningitis in a girl aged 3½ years remarkable for the fact that nuchal rigidity was absent throughout the three months' duration of the disease. The diagnosis was based on the presence of meningococci in the purulent cerebrospinal fluid and the symptoms of irritability, vomiting, and deafness. There was no autopsy.

In a discussion of *cerebrospinal fever in old age*, Pierron comes to the following conclusions. (1) Cerebrospinal fever after the age of sixty chiefly occurs in a sporadic form; (2) The clinical picture at this age is characterized by an insidious but occasionally apoplectiform onset, headache, vomiting, ocular symptoms, such as ptosis, nystagmus, and paralysis of the oculomotor nerve, and a more or less complete or intermittent coma. Transient paralyses may occur. Kernig's sign appears early, and is very pronounced. Nuchal rigidity is ill-marked, and may be entirely absent. (3) Owing to the latency of the symptoms, and the difficulty of diagnosis, cerebrospinal fever is probably more frequent in old age than statistics indicate. (4) In a comatose patient over 60, who presents the slightest sign of meningeal irritation, immediate lumbar puncture is required, as in this way alone can the diagnosis be settled and the prognosis rendered less gloomy by an early and active treatment. The gravity of the prognosis of cerebrospinal fever in old age is shown by a comparison of the mortality rates at different ages: in the infant under two years 42·3 per cent., from three to five years 26·7 per cent., in the adult 39·4 per cent., and in old age, 80 per cent. Pierron reports six cases in persons aged from 59 to 72, all of which were fatal.

Le Dentu records two cases of cerebrospinal meningitis in adults, aged 22 and 33 respectively, who presented unusual complications. In the first case the lesions as verified by autopsy gave rise to *external hydrocephalus* from hypertension of the cerebrospinal fluid as a whole, and also to internal hydrocephalus due to ependymitis and blocking of the ventricles. In the second case the latent infection determined *motor aphasia and facial palsy* which appeared and disappeared simultaneously, finally reappearing

before death, being probably due to pachymeningitis followed by encephalitis, though no autopsy was performed to confirm this diagnosis. Le Dentu suggests that in cases in which Kernig's sign is ill-marked, nuchal rigidity should be explored at the same time, one hand keeping the legs extended on the bed by pressure on the knees, while the other hand presses the occiput forward. In cerebrospinal meningitis flexion of the head considerably increases the difficulty of extending the legs, as pressure on the knees is more painful when this method is employed.

Allan records a *second attack* of cerebrospinal fever after an interval of eighteen months. Complete recovery took place under repeated injections of serum. He favours Herrick's suggestion that, in addition to passive immunity conferred by serum, active immunity should be stimulated by the use of meningococcic vaccine.

Chatt also reports a second attack in a boy aged 14, who had had an attack 10 years previously. In the first attack the strain of the meningococcus could not be determined, but it was probably of the A type. In the second attack the C type of meningococcus was found. Chatt therefore regards a difference in the strain of the meningococcus as an important factor in the causation of second attacks of cerebrospinal fever.

Edelmann describes the following *new sign* which he has observed at an early stage of cerebrospinal meningitis. On flexing the lower limb at the hip-joint with the knee extended, as in eliciting Lasègue's sign, dorsal flexion of the great toe frequently occurs as in Babinski's sign. This sign is apt to be found in senile cerebrospinal meningitis, in which nuchal rigidity and Kernig's sign are sometimes absent. It is also present in cerebral oedema.

Shearer and Parsons confirm Levinson's discovery that there is a marked *acidosis of the cerebrospinal fluid* in cerebrospinal fever, and consider that this acidosis in meningococcal infection, in contrast to what is found in other meningeal infections, is probably due to the ease with which the meningococcus can break down the glucose in the cerebrospinal fluid, forming lactic acid. They suggest that the striking difference frequently seen between the clinical symptoms and the number of meningococci present is due to the degree of acidosis. If the spinal fluid contains less than the normal amount of glucose, or the particular strain of meningococcus is unable to form the usual amount of acid, the fluid will show but slight change in reaction from the normal, although numerous meningococci may be present. In such cases the absence of any marked acidosis in the fluid would account for the mildness of the clinical symptoms.

According to Milesi, one of the most frequent symptoms of cerebrospinal meningitis is *affection of hearing*. The deafness which is fairly frequent in cases which recover lasts for several weeks and sometimes for ever. Milesi records a fatal case of cerebrospinal meningitis in a man aged 28 in whom the auditory nerve was found at the autopsy to present very severe lesions, the nerve-trunk and not the nerve-sheath exclusively being affected.

Sabrazès and Colbert state that the frequency of *meningococcus arthritis* varies with the age of the patient and the particular epidemic, being 2·4 per cent. in the child, 6·6 per cent. in the infant, according to Netter, and 15 to 22 per cent. in the adult (Sainton and Maille, Lafosse). In a series of cases observed by Sabrazès consisting of 219 adults, most of whom were aged 18–30 and a few 30–48, the proportion of joint complications was 5·26 per

cent. Out of 11 patients the right knee was affected in 8, or in 4·2 per cent. In one case the arthropathy preceded the meningitis; in three cases it accompanied it; in seven it appeared in convalescence; in three cases it was the arthralgic form, and in eight cases the form was accompanied by an effusion into the joint. Since 1916 Sabrazès has observed an almost equally large number of cases of cerebrospinal meningitis in which the percentage of joint complications was lower still. The writers record two cases illustrating the predisposing influence of typhoid vaccination on meningococcus carriers. They contrast the curability of meningococcus synovitis with the chronic synovitis due to tuberculosis and other causes, and emphasize the good effect of intra-articular injections of serum, and in protracted cases of washing out the joint with warm saline solution associated with congestion treatment.

Huebschmann, of Leipzig, describes the first case on record of *acute glomerulo-nephritis* due to meningococcal infection, the patient being a soldier aged 18 who died of cerebrospinal fever after two days' illness, and *post mortem* presented glomerulo-nephritis in addition to purulent cerebrospinal meningitis.

Dumont and Baron report a very severe case of cerebrospinal fever complicated by *urethritis and orchitis* in a man aged 40 who had never had gonorrhoea. The causal organism, which was found in the cerebrospinal fluid and the urethral pus, was a parameningococcus. Complete recovery took place under polyvalent antimeningococcal serum administered intrathecally and intravenously.

According to Bonnamour, of Lyons, who records an illustrative case, contrary to what occurred in the United States during the epidemic of 1805–11, in Ireland in 1866–7, and in Germany in 1886–7, *purpura* in cerebrospinal fever was until recently very rare in France, where it appears to have been noted for the first time in 1902 by Rist and Paris. Subsequently, and particularly since 1909, its frequency has decidedly increased, so that Netter found it present in 18 per cent. of his cases in 1913, and in 20 per cent. in 1917. It was first observed at Lyons during the war among soldiers, but it remained rare in the civilian population. Purpura may occur at all stages of cerebrospinal fever. It most frequently appears between the second and fifth day of disease, but it may precede the meningitis or, as in Bonnamour's case, be almost the only symptom of cerebrospinal fever which is not recognized until the autopsy. In rare cases purpura may occur by itself without any meningeal localization in association with septicaemic phenomena such as arthritis, fever, and constitutional disturbance.

Lereboullet and Cathala maintain that *meningococcal septicaemia* is not a rare occurrence, and that within the last few years cerebrospinal fever has frequently assumed a purpuric and septicaemic character. It may appear as a simple infective purpura with a clinically benign course until the development of the grave meningeal symptoms of the final stage. Every rheumatoid purpura, therefore, whose origin is not obvious, should be suspected as being possibly due to a meningococcal infection which may sometimes be detected by a blood culture and lumbar puncture. The writers adopt the following classification of meningococcal septicaemia proposed by Blanchier in 1898: (1) meningococcal septicaemia without meningitis running a fulminating course within a few hours or days, or on the other hand of a protracted character associated with relapses; (2) clinically latent meningococcal septicaemia and meningitis, as in a case

recorded by the writers; (3) meningococcal septicaemia with secondary spinal meningitis; (4) purpura accompanying cerebrospinal meningitis. This forms the largest group of cases, and the diagnosis is relatively simple.

Morgan reports two cases of chronic meningococcus septicaemia in men aged 28 and 33 respectively, who were rapidly cured by intravenous and intraspinous serum treatment.

Bourges, Rouiller, and Jobard report a case of meningococcus septicaemia without any meningeal or visceral localization in a man aged 21, who presented the triad of symptoms characteristic of meningococcal infection, viz. febrile attacks simulating malaria, arthralgia, and successive crops of a papulo-nodular erythema followed during the period of apyrexia by an attenuation if not disappearance of the arthralgia and the eruption. The case was cured by subcutaneous autovaccine therapy.

Delahet records a case of *seric meningitis* (vide *Medical Science*, 1919, **1**, 139–40) successfully treated by antiseric vaccination, which consisted in (*a*) subcutaneous injection of a mixture of equal parts of the patient's cerebrospinal fluid and horse serum; (*b*) intrathecal injection of the patient's own blood serum. He recommends that in any case of cerebrospinal fever which does not respond to the ordinary treatment, and in which the prolongation of the disease cannot be attributed to the persistence of meningococci or to encysted meningitis, serum treatment should not be continued until an examination has been made with Fehling's solution, which, according as it shows an excess or defect of glucose, indicates inflammation and therefore infection, or on the other hand irritation, i. e. seric meningitis.

The *medico-legal importance* of latent cerebrospinal fever is discussed by Pillot who records the case of a soldier who met with an accident (a fall off a bicycle), when he was already suffering from the disease. In this case the trauma does not appear to have aggravated the pre-existing condition.

Prophylaxis. Taylor, senior medical officer of the Uganda Protectorate, employed applications of tincture of iodine mixed with an equal quantity of native honey to the tongue of contacts two or three times daily as a prophylactic against cerebrospinal fever and influenza during an epidemic of these diseases in the Mbarara and Kigezi districts of Uganda in 1918–19. The rationale of the treatment was as follows: (1) the local disinfectant action on application near the site of infection, which in both diseases appears to be the respiratory passages; (2) the action of the increased flow of saliva which in itself is prohibitive to the growth of micro-organisms; (3) the action of iodine after absorption; (4) the excretion of the iodine in the saliva and respiratory passages acting as a disinfectant.

Treatment. Sharp, of Buffalo, N.Y., states that during an epidemic of meningococcus meningitis in 1916-17 a few cases occurred in which the purulent fluid was obtained with difficulty owing to adhesions or blocking of the vertebral canal. Injections of half-strength normal saline diluted the fluid and broke down adhesions, permitting a free flow of the purulent fluid. In some of these cases oxygen was injected and an additional flow of purulent fluid was evacuated before injection of antimeningococcal serum. During the last five years Sharp has treated 30 cases of meningococcus meningitis as well as other forms of meningeal infection by pneumorachis or intraspinal injection of oxygen after lumbar puncture. Although only the severe and apparently unfavourable cases were treated by this method, only 7 died and 23 recovered—a mortality of 23 per cent., which contrasts favourably with that of cases treated by antimeningococcal serum alone.

Sharp points out that the oxygen has very little, if any, effect in destroying the organisms, its action being largely mechanical in displacing the fluid and opening up secluded pockets of adhesions.

A detailed account of antimeningococcal serum therapy, as well as of all other aspects of cerebrospinal fever, will be found in Dopter's recent monograph on meningococcal infection.

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J. D. R.

CHANCROID

Symptomatology. Bagou has collected from the literature 76 cases of *chancroid of the hand*. He remarks that the condition is a rare one, as are all extragenital chancroids; that the index finger is the most common situation; that a breach of epidermis is necessary; that the lesions differ from chancroids of the genital organs in being seldom multiple; that the great majority of cases are due to auto-infection from the genital organs, but some cases to professional contamination, and that a few are caused by mediate contamination by soiled linen, &c. According to Bagou, no true case of phagedaena has been recorded in chancroids of the hand; nor one of 'mixed chancre', chancroidal and syphilitic. The differential diagnosis from whitlow is sometimes difficult, but the latter is more painful, causes more inflammatory swelling, and is less localized. Other lesions with which chancroid may be confounded are syphilitic chancre, syphilitic perionyxis when situated round the nail, tertiary syphilitic ulceration, tuberculous ulceration, ecthyma, and chilblain. The diagnosis often depends on microscopical and cultural examination for the bacillus of Ducrey.

Gougerot is of opinion that *chancroidal bubo* may develop not infrequently without any chancroid being discovered. He reports four cases in which not only was the chancroidal bubo the first lesion observed, but secondary syphilis also followed. Ducrey's bacillus was found in the buboes. In all these cases the date of appearance of secondary syphilis corresponded to double infection with Ducrey's bacillus and the spirochaete of syphilis.

Dujardin and Ducré report a case of *extragenital chancroid* of the tongue occurring simultaneously with one on the glans penis. There were typical buboes in the submaxillary region and in the groin, and Ducrey's bacillus was found in both chancroids. According to Dujardin only 15 cases of extragenital chancroid have been published.

Diagnosis. Thibierge and Legrain discuss the value of the Wassermann reaction in the diagnosis of chancroid and of 'mixed chancre' due to simultaneous infection with the bacillus of Ducrey and *S. pallida*. They remark that cases diagnosed as chancroid and confirmed by the presence of Ducrey's bacillus are not infrequently followed by secondary syphilis without undergoing transformation into chancres having the characteristic features of syphilis. Hence the importance of any aid in diagnosis. Search for *S. pallida* in chancroids is difficult. Since January 1920 these observers have applied the complement-fixation test to all cases of chancroid, using the original technique with congenital syphilitic liver as antigen. Out of 104 cases 22 were positive and 82 negative when first seen. Of 26 negative cases which came for a second test only one became positive, after an interval of six weeks. Of the 22 positive cases 3 had had antecedent syphilis and 3 presented syphilitic symptoms; these were obviously cases of chancroid occurring in syphilitics. But, in the case of the remaining 16, in which there was no history or sign of syphilis, the question of mixed chancre, or double infection, arose. According to Thibierge and Legrain the incubation of syphilitic chancre is from 18 to 22 days, and the Wassermann reaction becomes positive from 15 to 20 days afterwards. Hence, the syphilitic part of mixed chancre takes from 17 to 21 days (allowing one day for the incubation of chancroid) + 15 to 20 = 32 to 41 days after the appearance of the chancroid to give a positive Wassermann reaction. Therefore, before diagnosing mixed chancre by means of this reaction, the result must be compared with the date of the chancre; if this is less than 33 days the syphilis is antecedent to the chancre; if more than 33 days it may still be the same or a mixed chancre, and remains uncertain till secondary symptoms appear.

Of the 16 positive cases mentioned above, the date was less than a month in 10, unknown and probably recent in 5, and six weeks in 1, so that only the last could have been a mixed chancre. The authors conclude that a Wassermann test should be done in all cases of chancroid as soon as they are seen, and repeated every one or two weeks till six weeks have elapsed. If there is no positive reaction before the 40th day, it is probably a case of simple chancroid.

Königsberger draws attention to the difficulties in the differential diagnosis of chancroid and syphilitic chancre from their clinical aspect alone. In order to demonstrate this point he examined 1,442 primary venereal sores. Only 173 of these (12 per cent.) presented the typical picture of hard chancre, but *S. pallida* was found in all but two (99 per cent.); these two cases were also negative to gland puncture, and the Wassermann reaction

remained negative three months after the sore had healed. The typical picture of chancroid, or *ulcus molle*, was presented by 459 cases (31·8 per cent.), but in 10 per cent. of these *S. pallida* was found. In 619 cases (42·9 per cent.) the signs of 'mixed chancre' were present, and 50 per cent. of these were positive for *S. pallida*. The remaining 191 cases (13·2 per cent.) were atypical, showing neither the typical signs of soft or hard chancre. These presented the form of erosions or of lesions resembling herpes, balanitis, or scabies. In 34 per cent. of these, however, *S. pallida* was found. Königsberger, therefore, concludes (1) that the clinical differential diagnosis between syphilitic chancre and chancroid is not tenable, for in 10 per cent. of 'typical chancroids' *S. pallida* was found, and in 1 per cent. of 'typical syphilitic chancres' no signs of commencing syphilis were present; (2) that the percentage of 'mixed chancres' is much greater than usually stated, and about half of these are syphilitic; (3) that in 34 per cent. of apparently harmless sores *S. pallida* can be found.

Treatment. Dupuy recommends Fontan's method of injecting *iodoform vaseline in chancroidal bubo*. The technique, somewhat simpler than in the original method, is as follows: a small puncture is made with a narrow bistoury and all pus is expressed; 10 per cent. iodoform vaseline, equal in quantity to the pus expressed, is then injected with a syringe. The vaseline is melted in a water-bath and injected just before it commences to solidify. Rest in bed is preferable, but not essential. After three or four days the vaseline is expressed; if it is found to be mixed with pus the injection is repeated. This method gives the best results in cases where suppuration has become definite, but is less likely to succeed in more advanced cases when the skin has become red and thin. In 15 cases treated in this way by Dupuy 13 healed within a week and 2 were failures. Dubreuilh and Mallein are quoted as having had 15 failures out of 106 cases, all the rest healing in a week. Failures are due to chancrelization of the orifice of puncture, to too large a puncture, or to the bubo being in a too advanced stage. Risk of iodoform poisoning is slight.

Dub recommends treatment of the early stage of chancroidal bubo by means of the *ethyl chloride spray*, a method introduced by Bockenheimer. This causes contraction of the vessels followed by active and then passive hyperaemia. The intense cold is said to destroy most of the streptobacilli which, owing to sudden dilatation of the lymphatics, enter the blood-stream and give rise to the formation of antibodies. The action is thus presumed to be twofold, local destruction of streptobacilli and general destruction of those remaining by autovaccine. The application should not exceed half a minute, and the treatment is repeated daily for a few days till the bubo subsides. Out of 19 cases treated in this way only one required subsequent puncture.

Bagou considers that the usual local antiseptic agents, perchloride of mercury, carbolic acid, silver nitrate, tincture of iodine, potassium permanganate, &c., have little effect in healing chancroids. The best local application is iodoform, either in the form of powder, bismuth and iodoform paste, or iodoform ether. The various substitutes for iodoform are of little value. Peroxide of zinc is also useful. Lévy-Bing claimed good results from a 10 per cent. ointment of novarsenobenzol, but Lebenthal states that the arsenobenzol compounds have no effect on the bacillus of Ducrey. The application of heat is beneficial, either by prolonged immersion in water at 40° to 50° C., or by directing a current of hot air at 45° C. on the lesion twice daily; the

bacillus being very sensitive to a rise of temperature. All surgical treatment should be avoided in chancroids of the hand. In the case of chancroidal bubo, the following treatment is that adopted at the Hôpital St. Louis: before suppuration has occurred, hot fomentations; after suppuration, puncture with a fine bistoury, expression of pus, light curetting with a fine curette, washing out with peroxide and afterwards with weak chloride of zinc solution; finally injection and distension of the cavity with liquefied bismuth-iodoform paste or xylo-iodoform oil. Most cases are said to be cured in a week by this method.

Queyrat has tried a modification of Pick and Jacobson's stain for Ducrey's bacillus as a *local application for chancroid.* The solution he uses consists of Ziehl's fuchsin 35 c.cm., aqueous solution of methylene blue 15 c.cm. This is applied daily, and the sore is also washed every four days with hydrogen peroxide and soap. Healing is said to occur in 15 to 30 days. The application is painless and free from odour, which is a disadvantage in iodoform applications. Queyrat also refers to the practice of treating all chancroids with arsenobenzol, recommended by Jeanselme on the grounds that many cases are infected with syphilis at the same time. He considers this practice to be wrong, and that no case should be so treated till syphilis is diagnosed. Cases of chancroid should be carefully watched with regard to the evolution of the sore and the inguinal glands; after 30 days *S. pallida* should be looked for by scarification of the periphery of the sore, and several Wassermann tests performed. In this way double infection will be detected without inflicting unnecessary treatment on non-syphilitics.

Stümpke has experimented with *vaccines* in the treatment of chancroid. He refers to the previous work of Bruck and Ito (1913), who reported good results in cases of chancroidal bubo with a vaccine prepared from Ducrey's streptobacillus; also to the serum treatment devised by Reenstierna (vide *Medical Science*, 1921, **4**, 220). The latter method, he says, has not been confirmed. With regard to vaccines, Stümpke found great difficulty in obtaining a pure culture of Ducrey's bacillus. The material was obtained by scraping the sore under local anaesthesia, and cultures were obtained on blood agar, but these were of low vitality, and had to be separated from diphtheroid bacilli, streptococci, staphylococci, and other bacteria. He only succeeded in obtaining a pure culture in 3 out of 26 cases. The vaccine prepared from these cultures was administered intramuscularly or intravenously at intervals of 3 or 4 days, in doses of 0·1 to 0·5 : usually not more than 3 or 4 injections were required. The sores began to heal after the first or second injection. Local treatment was omitted till the specific characters of the sore had disappeared, when simple boric ointment was applied. The effect on chancroidal buboes was uncertain, as there were not enough cases to decide this point. Stümpke considers that the difficulties of culture must be overcome before vaccine treatment for chancroid can come into general use.

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C. F. M.

ABSTRACTS

SURGERY

Moynihan, Sir B. The surgery of the spleen. *Brit. J. Surg.*, Jan. 1921, **8**, 307.

This review commences with some very interesting accounts of the earliest recorded cases of splenectomy, and gives a brief description of experimental work in the same direction which was carried out between 1669 and 1841. The experiments proved conclusively that splenectomy was not a fatal operation, and it is of interest to note that Vulpius in 1894 found that splenectomy was followed by a transitory decrease in the number of the red and in increase in the number of the white corpuscles. The first operation in this country was performed by Spencer Wells in 1866. In 1898 Vancerts had collected records of 274 cases with 170 recoveries. Sir B. Moynihan quotes statistics from the Mayo Institute showing that up to September 1920 there had been performed at that time 73 splenectomies for splenic anaemia, with a mortality of 12·3 per cent.; 53 for pernicious anaemia, with a mortality of 5·6 per cent.; 26 for myelogenous leukaemia, with a 3·8 per cent. mortality; and 32 for haemolytic icterus, with a mortality of 3·1 per cent. There were other smaller groups, making in all a total of 243 splenectomies with 26 hospital deaths.

The historical section is followed by a discussion of the functions of the spleen, and an account is given of the anatomy of the blood-supply. The author regards all the cells of the pulp other than those which are purely supporting as belonging entirely to one category—that of modified endothelial cells. The cells here are supplied by venous blood and differ considerably from the pure lymph cells of the Malpighian bodies, which are supplied by arterial blood and give rise to a progeny of pure lymphocytes. He says there is a certain amount of evidence to show that the blood from the spleen does not mix freely in the portal vein with the blood coming from the superior mesenteric veins.

Even when allowances are made for the differences due to the varying reasons for performing splenectomy, there remain certain changes in the blood which are also found in splenectomized animals. There is a temporary anaemia gradually subsiding in approximately two months' time, and an increase in the leucocytes, whose numbers return to normal very slowly. At the end of a year this is replaced by an eosinophilia. There is no real evidence that the patients after splenectomy show an increased liability to infection. There is also an increased resistance of the red blood-corpuscles which are found to be less readily haemolysed after the operation. This may be due to the fact that the spleen makes a substance which weakens the red cells prior to their being engulfed by the phagocytes. After

splenectomy the amount of bile pigment that is formed is at first approximately only one-half of that which was formed prior to the operation. There is little or no evidence that the spleen manufactures a haemolysin. There is evidence to show that the spleen secretes a substance capable of stimulating the bone-marrow, thus accounting for the rapid anaemia that follows splenectomy, and that a substance is formed that inhibits the formation of white cells. There is also reason to believe that the spleen stimulates the gastric glands to produce more pepsin. He lays stress upon the fact that the spleen must not be regarded as an isolated organ, but that it is intimately connected with: (1) the haemopoietic system; (2) the reticulo-endothelial system; (3) the digestive system; (4) the sympathico-endocrine system.

The pathology of splenic diseases is discussed on the basis of the different functions of the spleen, and it is shown that the pathological changes may be considered in the three following groups: (1) there is a local reaction similar to that found in other organs—for instance, an abscess or a tubercular area; (2) the organism lodges in the spleen and produces a diffuse fibrosis such as is seen in malaria and syphilis; (3) various toxic substances reach the spleen and may either set up local changes there or pass on, perhaps being augmented by the toxic products of degeneration or over-activity of the existing splenic cells. These poisons may cause anaemia, may bring about haemolysis, or may excite fibrosis, especially in the liver. The individual symptoms which are thereby caused are then discussed in full, after which consideration is given to those diseases which have been treated by splenectomy.

Pernicious anaemia. A short historical survey of the descriptions of this disease is given and the condition shown to be due to an abnormally increased cell-destruction. Splenectomy has been urged because some observers have found that the operation is usually followed by a polycythaemia. The operation has now been widely performed, but, as Sir B. Moynihan points out, the results show that the mortality of the operation was high, that the immediate benefit which only seldom followed was transient, that post-operative complications were frequent, and that the general course of the disease was not altered. W. J. Mayo has shown that the results are greatly improved by combining with the splenectomy massive blood transfusions, which overcome the anaemia and stimulate the production of new blood, and the radical removal of local foci of infection.

Leukaemia. Leukaemia may be considered as a morbid process manifesting itself diffusely and consisting of hyperplasia of various leucocytes—sometimes of the lymphocytes, sometimes of the myeloid cells—scattered through the body. There are cases, however, in which the newly-formed cells are found in the spleen, lymph glands, and bone marrow, but do not enter the blood-stream. The author shows that splenectomy when the spleen is large is a most fatal and unsatisfactory method of treatment, but if it be undertaken after the use of radium the results, as shown by the Mayo statistics, are very much better.

Hodgkin's disease. In this condition splenectomy has been very rarely performed. Sir B. Moynihan has performed it in one case after the use of radium; the patient is alive and well twenty-two months after the operation, but it is doubtful whether the removal of the spleen has had any effect.

Splenic anaemia. Banti's disease. A description of this disease is given, and stress is laid upon the three changes which Banti originally

described: (1) where the spleen is enlarged and there is a secondary anaemia—this may last from three to twelve years; (2) the liver is enlarged and the amount of urine undergoes progressive diminution; the duration is brief; (3) the liver has gradually shrunk in size, and ascites appears, the symptoms being those of an atrophic cirrhosis; the duration is between one and two years. Banti regards the condition as being due to an infection causing a primary splenomegaly, and the spleen then produces another toxin which leads to the secondary changes. The cause of the infection is unknown, but a wide discussion follows as to the possibility of different infections. The only treatment for this variety of the disease is splenectomy, but even here, if the spleen be very large, it is wise first to try the effect of radium. The operation should be carried out as early as possible, for in the late stages of the disease the mortality is much greater.

Haemolytic jaundice. The characteristic of this disease is that it frequently occurs in several members of the same family and may extend over several generations. Occasionally, however, there appears to be no family history, and the disease seems to be acquired. The symptoms of the two types are very similar. There is acholuric jaundice, enlargement of the spleen, and anaemia. It is pointed out that the condition very closely resembles a cholangitis due to a calculus. The congenital form is often exceedingly chronic and although the patient has known of the jaundice, but little attention is paid to it. The acquired form runs a more rapid course. Splenectomy as in the last group has proved to be as specific, but in the very mild cases it may not be necessary to resort to this. After operation the improvement is swift and striking although there still remains an increased fragility of the red blood corpuscles. A. J. W.

Mayo, W. J. Relation of chronic fibrosis and thrombo-phlebitis of the spleen to conditions of the blood and of the liver. *Arch. Surg.*, 1921, **2**, 185.

The author lays stress upon the fact that the spleen has few functions which can be determined accurately. It has no known internal secretion. It originates certain rhythmic contractions, noticeably during the digestive period. The spleen apparently acts in conjunction with the liver, and may initiate certain processes. These functions may be regarded as three: (1) the filtering of micro-organisms and toxic substances from the blood; (2) the production of lymphocytes; (3) the destruction of worn-out red corpuscles.

He believes that the splenomegaly which occurs in chronic sepsis, typhoid, tuberculosis, malaria, syphilis, and kala-azar is the result of the inability to send sufficiently rapidly to the liver, for destruction, the micro-organisms which the spleen has caught and is unable itself to destroy. A number of the chronic splenomegalies appear to be due to the hibernation of micro-organisms in the spleen, where, for some unknown reason, they may become more or less immune, and later may be a source of general reinfection. Even if the micro-organisms eventually die, the changes in the spleen are permanent and the organ may continue unnecessarily to destroy the red cells and cause a grave secondary type of anaemia, a true splenic anaemia, which at the time of subsequent discovery would be of unknown origin. The effect of the different organisms on the spleen is the production of fibrosis and thrombophlebitis. The terminal portal cirrhosis of the liver

might be called a tertiary lesion resulting from the splenic anaemia. He says it should be borne constantly in mind that the basic pathology of the spleen—that is, generalized fibrosis and thrombophlebitis resulting in secondary anaemia and liver changes—is essentially the same as the splenomegalies of known aetiology, such as syphilis, and, in order to cover our ignorance of what the primary cause may be, we assume it is due to toxins. He points out that the cirrhosis of the liver which occurs as a terminal stage of splenic anaemia, and is then usually called Banti's disease, does not differ in any important respect from cirrhosis of the liver found with chronic alcoholism. The explanation of the improvement which follows splenectomy may lie in the fact that the toxins are diverted from the liver, although at present we have no knowledge as to whither they are diverted. It may be that the chronic fibrosis and vascular changes in the spleen produce the agent which acts detrimentally on the liver.

Johnstone, working in the Mayo Foundation, found that splenectomy was immediately followed by a very active leukogenesis, which may persist although gradually decreasing, from one to three months. Erythrogenesis is at first dormant but later becomes more active. The results of splenectomy in man have been much disputed. Some of the observers claim to find polycythemia, while others found a secondary anaemia which persisted for three to four months. A. J. W.

Connors, J. F. Ruptured spleens: spontaneous and subcutaneous. *Ann. Surg.*, 1921, **73**, 1.

In spite of the fact that the spleen is anatomically well protected, a review of the literature reveals a large number of cases of spontaneous rupture. The injury causing such has often been slight. Connors, in his review of past reports, states that Planson in 1909 compiled 140 splenectomies with a mortality of 37·1 per cent. A brief description of the functions of the spleen is given. After splenectomy there is an increase in the endothelial cells of the lymphatic glands which are phagocytic to red cells. Ascher has shown that the spleen contains a substance which is but slightly haemolytic when acting alone, but when acting in conjunction with a liver extract forms a very powerful haemolytic agent. Halliburton claims that the spleen aids in the formation of leucocytes because he found a greater number of white blood corpuscles in the splenic vein than in the artery. It is thought that during digestion the spleen acts as a reservoir for the portal system as it begins to enlarge after a meal. In nearly all infections the organ is enlarged, and Morris and Bullock have shown that dogs will progress well without the spleen unless they are put to the strain of resisting an acute bacterial invasion. It is thus believed that the human body is more susceptible to infection. He comes to the conclusion that after splenectomy there is an increase in the leucocytes, especially in the mononuclears. The erythrocytes decrease in number but gradually increase with the increase in the percentage of haemoglobin. A moderate eosinophilia occurs some months after the operation, and may persist for a considerable length of time. In many of the reported cases the operation has been followed by a severe infection of the abdominal wall.

The subcutaneous ruptures are caused by all varieties of contusions, blows, and falls. They all show extreme shock and have signs of internal haemorrhage, and the only treatment is immediate operation. Better

results have been obtained after the use of direct blood transfusions. The author reports at length six cases, five of which recovered. He also reviews cases of spontaneous rupture and reports at length a case of his own. He comes to the conclusions: (1) that the loss of the spleen makes no difference in the physical welfare of these patients; (2) the blood picture at the last blood examination revealed but a slight deviation from the normal; (3) the presence of accessory spleens must be considered an important factor; (4) direct blood transfusion is a great help in the successful outcome of these operations. A. J. W.

Fowler, R. H. Surgery of cysts of the spleen. *Ann. Surg.*, 1921, **73**, 20.

This article is a continuation of the author's previous reviews of published cases of cysts of the spleen. He finds no reason to alter his previous classification into (1) dermoid cysts; (2) non-parasitic cysts; (3) parasitic cysts.

Dermoid cysts. There are but two authentic cases on record, the second of which was reported by Kummaris. The patient, a woman aged 40, had had a swelling of the abdomen for five years, which was diagnosed as an ovarian cyst. At operation the cyst was found to spring from a dislocated spleen and owing to firm adhesions could not be removed. It was therefore punctured and found to contain a litre of peculiar fluid containing a number of round, white, shot-like balls and a large quantity of hair.

Non-parasitic cysts. This group is subdivided into true cysts and pseudo-cysts. The latter may be either traumatic or degeneration cysts, and the true cysts may be due to (1) inclusions of peritoneum; (2) polycystic disease; (3) neoplastic.

A review of the literature from 1912 to 1921 reveals five cases reported by four observers. Fowler states that the majority of this variety of cyst appear between the ages of thirty and fifty, and only two were found in infants under one year. Females were more frequently affected than males. Occasionally there seems to be a relation between pregnancy and cyst formation. Antecedent diseases of the spleen may also exert an influence, especially malaria and syphilis, perhaps because the organ is more prone to become the seat of a haematoma. The most generally acknowledged factor in the aetiology is trauma; a history of injury was obtained in nineteen cases, but in some of these the interval between the injury and the discovery of the cyst was twelve or more years. In two cases the pedicle of the spleen was twisted, but this may have followed the formation of the cysts rather than have been a cause.

Nothing has been added in recent years to the knowledge of the origin of the pseudo-cyst. In thirty-four of the forty-four cases rupture of the blood-vessels, spontaneous or traumatic, figures most conspicuously. A large unilocular cyst probably arises secondarily from a subcapsular haematoma.

Small multiple surface cysts may originate from the infoliation of peritoneal endothelium and are hence known as infoliation cysts. It is possible that trauma is not essential for this process and that multiple small ruptures of the splenic capsule may ensue from a rapid swelling of the organ. Pepere believes that the so-called serous cysts originate from cellular nests, which remain under the splenic capsule from abnormal invaginations of the perisplenium during development of the organ. Polycystic disease is best

explained by the dilatation of the blood or lymph sinuses. In the case of lymphatic cysts resulting from lymphangiectasis, the organ is enlarged as a whole. The surface is irregular and the seat of countless projections. The cut surface shows innumerable cavities, some isolated, others confluent. The latter in their interiors present interlacing networks giving the characteristic appearance of multilocular cavities.

Fowler says the symptoms are in no way characteristic. When the cysts are small they cause no symptoms and the condition is found accidentally *post mortem*. Large cysts cause symptoms of pressure. The predominant symptom is pain. The tumour is usually located to the left of the umbilicus and has frequently been mistaken for a movable kidney. It may extend to the median line and below the navel, and the mass may be freely movable or fixed. A diagnosis is rarely made clinically. The treatment has consisted either of puncture, incision and drainage, excision of the cyst or splenectomy.

Parasitic cysts. These are uncommon. That due to *Taenia echinococcus* is the most frequent variety and occurs in regions where hydatid disease prevails. The spleen was involved in 2 per cent. of the cases of hydatid disease studied by Thomas. He collected eighty-eight cases of hydatid of the spleen, in forty-five of which this viscus was alone affected. The cysts may be unilocular or multilocular. The mortality of twenty-three cases of splenectomy for these cases was 17 per cent. A. J. W.

Peck, Charles H. Cavernous haemangioma of left lobe of the liver. *Surg. Gynec. & Obstet.*, 1921, **33**, 277.

Peck records the case of a woman, aged 34, from whom he successfully removed a haemangioma weighing 3 pounds 14 ounces, by extirpating the left lobe of the liver.

For about a year she had noticed gradual enlargement of the abdomen and had suffered from vague abdominal discomfort, occasional pain, flatulence, constipation, and from a loss of 22 lb. of weight.

There was a large, soft, smooth, elastic, insensitive, mobile tumour in the epigastrium, extending from ensiform cartilage to umbilicus. X-ray examination showed the stomach displaced to the left.

At operation the mass was found to be deep-purple, smooth, soft, elastic, and free from adhesions; to the right the lobe had been stretched and thinned by the drag of the weighty tumour. Total excision of the pedunculated left lobe was done, the vessels in the pedicle being secured by clamp and ligature as it was divided, step by step; then the cut edges of the stretched left coronary ligament were sutured together. The tumour weighed 3 lb. 14 oz. and occupied the entire left lobe.

Microscopic examination showed it to be a cavernous haemangioma with much replacement of liver-tissue. During convalescence the patient had three attacks of sharp pain in left thorax, cough, fever, and blood-stained sputum, but no infarct or consolidation of lung was seen with the X-rays. She also had a mild phlebitis of the right leg. She is now quite well. The tumour measured 26 by 9 cm.

The author refers to a number of other recorded cases, paying special attention to those treated by operation. The largest recorded weighed 37 lb. at death. He cites the cases of Mantle and Chiara, in which death took

place from haemorrhage within 2 and 1 hours, respectively, of exploratory operation.

He has collected 17 cases of excision of hepatic haemangiomata, with 15 recoveries and two deaths. Fifteen were in women and two in men. The left lobe was affected in 11, the right lobe in 7, and the spigelian in 1; one case showed multiple tumours; in the other the site was not stated. The largest excised tumour (Pfannenstiel) weighed 5 lb. when collapsed, and probably double that weight when full of blood; in this case operative haemorrhage was very severe, but the patient ultimately recovered.

The methods of controlling haemorrhage during the operations have included elastic ligature, chain ligature through pedicles, cauterization, and packing. Keen in one case formed an artificial pedicle by incising the liver on each side of the growth and then applying an elastic ligature and packing the wound open. The author gives a bibliography referring to 27 articles.

C. C. C.

Balfour, D. C., and **Ross, J. W.** **Post-operative biliary fistula.** *Archives of Surgery*, 1921, **2**, 582.

Two types of biliary fistula may be recognized, spontaneous and post-operative. The spontaneous are rare and may open externally at various points on the chest or abdominal wall, but are most frequently seen at or near the umbilicus. They may communicate internally with almost any part of the gastro-intestinal tract, a bronchus, the right kidney, or the urinary bladder. Failure of a post-operative fistula to close spontaneously means that some obstruction prevents the bile from flowing along its normal course. This is usually due to faulty surgery, and repair of the fistula may offer serious difficulties. The authors review a series of 166 cases of biliary fistulae seen in the Mayo clinic between January 1, 1910, and December 31, 1919. Of these 166 cases, 105 were due to stones either in the gall-bladder or ducts, twenty-two to recurrent cholecystitis, thirteen to division of the common duct, and eleven to strictures of the common, hepatic, or cystic ducts. Only 10 per cent. of them had had the gall-bladder previously removed. They claim that this emphasizes the importance of removing the gall-bladder at the first operation. With cholecystostomy there is more risk of performing an incomplete operation or of overlooking the pathological condition, but cholecystectomy increases the danger of injuring the common or hepatic ducts. Such a complication should, however, be very rare; its rarity with proper technique in the cholecystectomy, is indicated by the fact that it only occurred in twelve of 9,009 operations upon the gall-bladder and ducts performed at the Mayo Clinic. In eleven of these the gall-bladder had not been removed. Of 5,997 cholecystectomies there was but one subsequent fistula, whereas with the 1,879 cholecystostomies there were eleven.

Among the causes of overlooking or producing conditions which divert the bile through the fistula inexperience in operating ranks high. The next important factor is an inadequate exposure at operation. Even apart from this the operation may be extremely difficult in a stout patient with a high-lying liver and inflammatory adhesions which prohibit a satisfactory exposure. Hurried operations and incomplete or careless exposure is also a frequent cause. The ducts should, in every case, be explored, even if the symptoms only point to stones within the gall-bladder. A contributory factor in 90 per cent. of cases in the authors' series was failure to remove the

gall-bladder. The most serious conditions are included under the heading of accidental injury to the ducts. The most important is division, crushing, or resection of a portion of the common or hepatic ducts, the chief causes of which are failure to identify the cystic duct and hurried attempts to grasp the bleeding cystic artery. Although there was no case in the series showing clear proof that the pressure of a drain was solely responsible for a fistula, it is conceivable that such a condition might arise. Finally the reformation of stones may be mentioned as a possible factor.

The indications for surgical interference depend to a large extent upon the length of time the fistula has been draining, on its behaviour from day to day, and on the cause and probability of its persistence. Ample time should always be allowed for the fistula to close spontaneously. If at the end of three weeks a large quantity of bile is continually draining through the incision and only a small amount is entering the intestine it may well be suspected that some mechanical obstruction exists. The recurring fistula which opens and closes spontaneously is suggestive of a ball-valve stricture. The length of time that the fistula may exist without affecting the general health of the patient will depend chiefly upon the amount of bile that is escaping. The longest time during which all the bile drained to the surface in their series was three years, and the patient showed no other recognizable nutritional disorder other than the anaemia.

The operative management varies within wide limits. The cure of a gall-bladder fistula by removal of a stone impacting the cystic duct is quite simple and satisfactory. On the other hand, nothing can exact more surgical ability and experience than an attempt to restore the normal course of bile after several previous efforts have been made to repair the ducts. Any calculi within the common duct should always be removed. The repairing of a biliary fistula due to an extensively damaged or excised common or hepatic duct offers the most difficult situation which may confront a surgeon. Experience has demonstrated that the most satisfactory and often the only method of dealing with such cases is to make a direct anastomosis between the hepatic duct and duodenum. In their series of 166 cases there were 16 deaths, a mortality of 10 per cent. In 35 cases of stone in the cystic duct there was no operative mortality, while, when there was division or stricture of the common duct, six deaths occurred in twenty-one cases. Of the 83 living patients from whom positive information could be obtained, 80 had been completely relieved of fistula, while 12 reported occasional attacks of pain and jaundice. A. J. W.

Fulle, G. B. C. Contributo sperimentale alle ferite della cistifellea e alla colemia sperimentale. [**Contribution to the study of experimental wounds of the gall-bladder and cholaemia.**] *Arch. ital. di chir.*, 1921, **4**, 229.

Five series of experiments on dogs and rabbits. The first and second, in which the fundus of the gall-bladder was removed, or a big wound, three or four cm. long, made in the wall, were to test the effects of free escape of bile into the peritoneal cavity; the third, in which a small wound, from 0·5 to 2 cm., was made, to ascertain the effects of slower or more limited escape of bile into the abdomen; the fourth, to determine the absorptive power of the peritoneum for normal bile; the fifth, to determine the toxicity of bile effused in the circumstances of the earlier series.

The results, whilst not agreeing entirely with those of previous

investigators, were almost entirely consistent in their own series. Thus all the animals in series one and two died in from 19 to 62 hours (dogs) or from 12 hours to 7 days (rabbits), whilst with the smaller wounds practically all the animals survived, after exhibiting in a minor degree the symptoms (refusal of food, oliguria, diarrhoea, loss of flesh) that preceded the fatal termination in the former.

The peritoneal reaction is pretty nearly inverse to the size of the wound, which, however, does not necessarily correspond to the amount of bile effused. With large wounds there are few if any signs, whilst with small wounds the local plastic reaction may be enough to isolate the wound and shut off the effusion. Intraperitoneal injection of ox bile and some clinical records alike show the very slight irritative effect of normal bile on the peritoneum, which is nevertheless stained by the bile pigments. It might be supposed that the small quantity of effused bile found in the abdomen of animals dying after a large wound was due to rapid absorption in the early stages, were it not that in none of the first or second series was there a trace of icterus and no evidence of bile pigments could be found in the urine of these cases, whereas in animals that survive small wounds evidence is forthcoming in the urine from an early period. Large doses of ox bile, given intraperitoneally, lead to no excretion by the kidneys, whilst small doses lead to such excretion constantly and early. Apparently, where absorption of toxic substances from the bile is rapid and massive, the effect on the kidney is to destroy the capacity for elimination of pigments, whilst the short period of survival excludes icterus.

Toxicity of normal bile, homologous or heterologous, is greater than that of the bile recovered from the peritoneum after effusion, possibly because the noxa are already absorbed, or possibly because the peritoneal effusion evoked is potent with antitoxic bodies.

In general it seems that the protective functions, competent if given time to neutralize the lethal influence of the biliary poisons, fail when the initial dose is large. The lethal effect may perhaps be exerted through disturbed hormone balance, and in particular through diminution or suppression of the suprarenal function. E. R. C.

Campbell, J. M. H. Acholuric jaundice. *Guy's Hosp. Rep.*, 1921, **71**, 274.

The present paper gives a brief *résumé* of the publications since 1890, which includes a description of the fragility of the red blood cells. Campbell describes a modification suggested by Ryffell which was used in the determining of the fragility in the cases he reports. He finds that with acholuric jaundice haemolysis begins at 0·66 to 0·60 per cent. NaCl and is complete at 0·5 per cent., whereas in the normal individual it begins at 0·45 and is complete at 0·36. This increased fragility is characteristic of acholuric jaundice and has made it possible to distinguish the disease clearly and sharply from all other conditions. There are two distinct types, the familial and the acquired, the former of which is also congenital. The acquired is more severe in its onset and the average red count is lower than in the familial form. Apparently the acquired form becomes in turn familial and congenital. Great improvement in the disease occurs after splenectomy, although the fragility may remain abnormal for longer periods after the operation.

A full history of two cases is given, one of which was treated by

splenectomy. The first case was an example of the familial type and a detailed account is then given of the family history, which dates back to the grandmother. Of her five children the fifth was alone affected and was in the London Hospital in 1897. Of the four normal children the eldest married a normal woman and they had twelve children. Of these twelve the fourth is the one quoted in the paper. The ninth was a definite case and the seventh was doubtful. The others were all healthy. Of the remaining three children of the second generation one had a normal son and the second had three sons and four daughters all normal. The third had eight children, of whom four were affected.

A review of the literature revealed that in a family which had been traced fifty-three members were affected out of a total of one hundred and sixty-three. Twenty-five were females and twenty-eight were males. In some cases the disease was transmitted through healthy parents and in some cases through parents who were themselves affected, and it is difficult to fit the condition in with the Mendelian theory. But few cases have been reported where the disease occurred in the fourth generation and there would seem to be a tendency for the disease to die out in this generation. All observers agree that the Wassermann reaction is negative.

There are two theories as to the cause: that either there is a primary deficiency in the red corpuscles which makes them abnormally fragile, or that the spleen is primarily at fault in destroying the corpuscles too readily. The fact that the washed corpuscles show abnormal fragility is evidence in favour of the former view. The good results of splenectomy favour the latter. Campbell states that the most likely view seems to be that, either from heredity or from some infection, the red corpuscles become abnormally fragile, and under these conditions they are haemolysed by the spleen in unusual numbers and the spleen hypertrophies on account of its increased work. In this way the anaemia and acholuric jaundice may be produced. After splenectomy the red cells cannot be haemolysed in large numbers.

Campbell lays stress upon the fact that in a large proportion of the cases gall-stones have been found in the gall-bladder, which suggests that they are dependent upon the repeated attacks of jaundice. A. J. W.

Lilienthal, Howard. Carcinoma of thoracic oesophagus: extrapleural resection and plastic. Description of an original method with report of a successful case without gastrostomy. [B.] *Ann. Surg.*, 1921, **74**, 259–79.

In 1913, Torek, of New York, succeeded in extirpating the tumour-bearing oesophagus from a woman over 60 years of age—by boldly invading the posterior mediastinum through the pleura. This patient is still alive, swallowing her food through an external tube of rubber which runs between an oesophageal opening in the upper thorax and a gastrostomy. But neither Torek nor others have succeeded in such an operation since then.

The greatest danger is infection of the mediastinum, whether the route of operation be transpleural or extrapleural.

Extrathoracic tubes of skin or of hollow viscera have been used to side-track the oesophagus, with many failures.

Lilienthal, in order to minimize risk of mediastinal infection, divides his operation into two stages; first, exploration and isolation of the oesophagus with obliteration of the mediastinum, and second, resection and plastic reformation.

Preliminary dissections were made on the cadaver and the questions considered to determine (*a*) whether the pleura could be stripped free with safety and (*b*) whether the oesophagus could be reached best from the left or the right of the spine. The author, in spite of a discouraging experiment on the pleura in the cadaver, decided that the operation was feasible and that the left approach would be simpler and safer than the right. His reasons for choosing the left approach were that (1) the descending aorta would form a good landmark, (2) the important veins and thoracic duct would be out of the way, and (3) the free pleural fold that crosses the medial plane from the right side would be avoided.

The writer gives a full history of the pre-operative conditions, the operative details, and post-operative treatment of his patient, the first to survive a complete extrapleural oesophagectomy. He also gives a synopsis of four other cases in which he explored the oesophagus through the mediastinum; all died, three of them through mediastinal infection due to injury to the diseased oesophagus in trying to isolate it.

The successful operation was conducted as follows: the obstruction shown by X-ray examination appeared to be in the lower part of the oesophagus.

Under nitrous oxide-ether anaesthesia the patient was placed on his right side with back bowed and lower limbs flexed; the bridge of the table was raised to cause a scoliosis with convexity to the left. By means of an incision beginning $1\frac{1}{2}$ inches to the left of the spine, running along the 8th interspace as far as the mid-axillary line and then turning downward back along the 10th rib, a flap with posterior attachment was turned back and wrapped in moist towels; it contained skin and subcutaneous fat chiefly. Then the greater part of the 9th rib was subperiosteally resected and, beginning posteriorly, the pleura was separated, by the finger, from the chest wall and then forward under the 10th rib, which was divided posteriorly near its angle. The pleura and lung were pushed forward, the great splanchnic nerve and aorta recognized and pleura readily separated from the latter. A stomach-tube was passed from the mouth through the oesophageal stricture; thus the oesophagus, which had been pushed forward with the pleura, was rendered more readily palpable.

No tumour being found in the lower part of the oesophagus, further exposure upward was got by separating the pleura from the 8th rib and resecting a short portion, and then by doing the same to 7th and 6th ribs; with a rib-spreader in position a fusiform tumour could then be felt from $1\frac{1}{2}$ inches below the aortic arch to a point 3 inches below it. The oesophagus was isolated and the right vagus separated from it (after a pledget of cotton wool soaked with 5 per cent. cocaine had been applied to the nerve). The oesophagus was lifted out of the wound by passing a thin rubber tube (as retractor) around it above and another below; the skin-flap was then passed in between it and the other structures and its tip coiled round the segregated oesophagus, so that the latter now lay in a skin-lined trough. The anterior part of the wound was closed and the rest of it left to heal by granulation.

The patient swallowed after the operation rather better than before it.

A fortnight later the *2nd stage* was undertaken under morphia, gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{150}$., with the patient sitting up and bending forward.

The oesophagus was drawn back by means of the two rubber-tubing retractors, which had been left *in situ* at the first operation, light adhesions

were broken down, and the oesophagus divided across above and below the growth.

The skin-flap had already formed a trough and the mediastinum was sealed off by it and by granulation tissue. After unsuccessful trial of a T-tube, a tube was passed from the wound down the lower part of the oesophagus, for feeding purposes, and another into the upper part to maintain patency. A week after the 2nd operation an Einhorn tube was passed from mouth to stomach and the patient fed through this.

3rd stage. A fortnight after the 2nd operation an attempt was made to close the groove by rolling the skin-flap over after division of its pedicle; the flap, however, persistently flattened out again. After a period of trouble due to this tendency and to contracture of the upper orifice into the oesophagus, successful dilatation of the canal and plastic flap closure of the groove was attained. The patient can pass a stomach-tube himself and it is intended that he shall continue to do so several times daily for a year to prevent contracture.

The operation is believed to be the first completed extrapleural resection of oesophagus. The pleura was not damaged except for one small accidental tear that was immediately sutured.

There is a full bibliography, and the paper is well illustrated.

C. C. C.

Eusterman, G. B., and **Senty, E. G. Benign tumours of the stomach.** *Surg. Gynec. & Obst.*, 1922, **34**, 5–14.

This is a report of 27 cases, which were confirmed by operation at the Mayo Clinic between 1907 and 1921. The proportion of simple to malignant tumours of the stomach noted during this time was about 1 to 200, the simple tumours representing 1·3 per cent. of operable tumours of the stomach; 17 of the 27 were found to be the cause of the patient's symptoms, the remainder being discovered accidentally. One-half of the patients were over 40. Of the symptoms which were due to the tumour, recurrent haemorrhage was connected with ulceration of the growth, pyloric obstruction was noted in 25 per cent., and attacks of pain simulating gall-stone colic in several cases of juxta-pyloric tumour. The largest group was formed by the myomata and fibromata.

E. K. M.

Nicolaysen, K. Pathologisch-anatomische und experimentelle Studien über die Pathogenese des chronischen Magengeschwürs. [**Pathologico-anatomical and experimental studies in the pathogenesis of chronic ulcer of the stomach.**] *Deutsche Ztschr. f. Chir.*, 1921, **167**, 143–263.

The material from which the pathologico-anatomical portion of this paper was obtained consists of 57 cases of gastric and duodenal ulcer, 28 of which were obtained at operation and 29 at autopsy. Out of 2,000 post-mortems at Christiania (1911–19) 4·5 per cent. showed active or healed ulcers. Gastric were more numerous than duodenal ulcers, in the proportion of 3 : 1. He notes that in gastric ulcers the cause of death is haemorrhage in 15 per cent., perforation in 5 per cent., while in duodenal ulcers the proportion is exactly reversed.

His account of the pathological anatomy of chronic ulcer is clear, but contains no new information. There is a detailed description of the chronic inflammatory changes of the various tissues of the stomach wall in the

neighbourhood of an ulcer, and a note on the frequency with which were found diverticula of the duodenum produced by the pushing out of the wall of the gut between adjacent scars of healed ulcers. The wall of this type of diverticulum is composed of all the coats of the duodenum in contra-distinction to the diverticula produced by the bulging of the thin scar of a healed ulcer. The first type occurred in three out of six cases. He considers that chronic duodenal ulceration is a more acute inflammatory process than chronic gastric ulceration, and instances in support of this view the slighter degree of histological change in the bases of the ulcers examined.

The experimental part of the investigation was carried out on dogs, in which the modification in the rate of healing of artificially produced gastric ulcers introduced by feeding with micro-organisms and by interference with the innervation of the stomach was studied in an attempt to throw light on the cause of chronicity. Gastric ulcers were produced by freezing the exposed stomach wall for 4–6 minutes with an ethyl chloride spray. The resultant slough, after digestion by the gastric juice, left an ulcer which healed rapidly, the latest date after freezing at which an ulcer was found unhealed being the ninth day.

In a second series of dogs an attempt was made to study the effect of infection on the rate of healing by feeding with cultures of an organism obtained from a human gastric ulcer and proved to be pathogenic to the animals employed, whether injected subcutaneously or into the blood-stream. The introduction of such cultures two to four days after freezing the stomach wall led to no appreciable delay in the healing of the ulcers. Nicolaysen concludes from this that infection of experimentally-produced ulcers throws no light on the causation of chronic ulcer in man.

In a third series both vagi were cut immediately below the diaphragm and the same technique of freezing followed. The dogs were killed at intervals of from 3 to 180 days after operation. The artificially-produced ulcers were found unhealed up to 22 days after operation, but were healed in every case from that time onwards. Nicolaysen concludes that vagus section has no effect on the rate of healing of experimentally-produced ulcers. He confirms the frequent appearance of spontaneous ulceration in vagotomized dogs as described by Litthauer, Van Ijzeren, Zironi, and others. These ulcers were frequently multiple and showed all degrees of activity and healing irrespective of the time which had elapsed since operation. The largest ulcers, and those which approximated most closely to the chronic type, were found along the lesser curvature.

Since artificially-produced ulcers heal as readily after vagus section as in the intact stomach, the healing process must be independent of vagus action. The fact that there is a constant tendency to the appearance of fresh ulcers in the vagotomized stomach suggests that there is a failure of the resisting power of the mucous membrane to the mechanical irritation of food or to the digestive power of the gastric juice, and this is confirmed by the observation of Van Ijzeren that such ulcers do not appear in the vagotomized animal after gastro-enterostomy.

Nicolaysen summarizes his theory of the evolution of a chronic ulcer by assuming a vicious circle in which inflammatory infiltration of the base of an acute ulcer leads to perineuritis and endarteritis, which in turn tend to retard the rate of healing. The circle is started by the delay in the healing of an acute ulcer induced by the mechanical and chemical irritation

of gastric contents. He claims that this explains the good effects of dietetic treatment and gastro-enterostomy.

NOTE.—The experimental evidence afforded by this paper is altogether too slender to carry so ambitious a conclusion as an explanation of the transition from acute to chronic ulceration. What the author has actually shown is that a particular type of artificially-produced ulcer heals as readily in the vagotomized as in the intact dog. He also confirms the observation of previous workers that ulcers appear spontaneously in the stomach after vagus section. His review of the experimental production of gastric ulcer is incomplete, e.g. he makes no reference to the work of Bolton. E. K. M.

WEBB, R. C. Disconnecting gastro-enterostomy stomata. *Surg. Gynec. & Obst.*, 1921, **33**, 681–6.

Two experiments were made on dogs to test the fate of portions of stomach wall transplanted to the jejunum, as in Andrew's method of disconnecting gastro-enterostomy stomata. Andrew pointed out that stricture might follow closure of the jejunum if a gastro-enterostomy was undone by cutting along the line of anastomosis, and suggested making the disconnecting incision in the stomach 1 cm. from the anastomosis, closing the opening in the jejunum by turning in the cuff of stomach wall so obtained.

Webb found that in two dogs examined 5½ months after disconnexion of a gastro-enterostomy by Andrew's method the transplanted gastric mucous membrane retained its normal microscopic appearance and staining reactions, and that there was no stenosis at the site of jejunal closure.

E. K. M.

UHLRICH, P. De la gastro-pylorectomie et duodéno-pylorectomie immédiates dans le traitement des ulcères perforés de l'estomac et du duodénum. [**The treatment of perforated ulcers of the stomach and duodenum by partial gastrectomy or pylorectomy.**] *Rev. de chir.*, 1921, **59**, 467–502.

After the first successful case reported by Brunner in 1903, there was no reference to this procedure until the last two years. From the literature of this period Uhlrich has collected reports of 31 operations, the detailed accounts of which make up the bulk of his communication. In this series were three deaths, a figure which suggests that the number of unsuccessful cases reported scarcely represents the true position of affairs. Apart from the collected case reports, the paper consists of an enthusiastic advocacy of the radical treatment of perforated ulcers by excision wherever the state of the patient renders this possible. Uhlrich adds no fresh cases to the literature. E. K. M.

NOWAK, E. Zur Technik der Duodenalresektion bei Ulcus Duodeni. [**The technique of resection of the duodenum for ulcer.**] *Arch. f. klin. Chir.*, 1921, **116**, 518–41.

After a short survey of the rise of resection into surgical favour in place of gastro-enterostomy, with or without pyloric exclusion, Nowak gives the results of 47 consecutive cases of resection of the duodenum for ulcer in von Eiselsberg's clinic. All the ulcers were above the papilla, those which were farthest from the pylorus showing a slight preference for the

posterior wall. The ulcers were multiple in 36 per cent. of the cases, and in no case was the ulcer healed. In 10 cases there was more or less duodenal stenosis.

The operation was completed in 34 cases by the method of Billroth I, in 13 by that of Polya. There was one death from haemorrhage and peritonitis in a wasted patient and one case of injury to the common bile-duct which necessitated a subsequent cholecystenterostomy.

Local anaesthesia was used, with infiltration of the small omentum and transverse mesocolon, reinforced where necessary by light inhalation anaesthesia. The duration of the operation was just over an hour in a simple case to three hours in a difficult one. A mid-line incision from ensiform cartilage to umbilicus is used and extended, if necessary, by transverse division of the right rectus 3 cm. above the umbilicus. Nowak has observed no failure of the blood-supply of the duodenal stump, whether closed or anastomosed to the stomach, and with the technique which he employs has no hesitation in separating duodenum from pancreas for 3 to 4 cm. in order to bring it up to the stomach. The free mobilization of the duodenal stump is an essential step in the performance of the Billroth I operation, since he follows Finsterer in removing $\frac{1}{2}$ to $\frac{2}{3}$ of the stomach in order to reduce the acidity of the gastric juice.

In freeing the duodenum from the pancreas he avoids the ligation of the superior pancreatico-duodenal artery and keeps close to the wall of the duodenum, tying the small vessels which pass from pancreas to bowel after division of the peritoneal reflection. To facilitate this step he introduces a grooved sound along which a blunt ligature carrier can be passed. If the duct of Santorini is encountered, it is divided between ligatures. The duodenum is separated from the pancreas for 3 to 4 cm. distal to the ulcer when the latter has not perforated the wall of the gut. If the ulcer has perforated into the pancreas, an attempt is made to free the duodenum both on the proximal and distal sides of the ulcer before attacking the latter direct. The adherent edges are then cut through, the base of the ulcer scraped with a sharp spoon to remove granulations and then covered with a free omental graft, or left to form adhesions if sufficiently closely covered by the site of the anastomosis. In avoiding the common bile-duct, the chief difficulty is met with in those cases where an adequate view of the field of operation is prevented by inflammatory thickening of the wall of the duodenum and the surrounding tissues, under which circumstances the duct is adherent to the bowel. The only precaution necessary is to keep close to the wall of the duodenum throughout, leaving shreds of muscle on the pancreas rather than trespassing into the substance of the gland. The hepatic artery is less often in danger, though it may be attached to the base of an ulcer of the posterior wall near the flexure, and on account of induration of the surrounding tissues its pulsations may not be recognizable to the touch. It can always be avoided by the same manœuvre of keeping close to the duodenal wall.

Nowak strongly advocates resection rather than gastro-enterostomy, with the reservation that, since resection of an adherent ulcer may take up to three hours, in patients who are poor operative risks the operation should be limited to cases where the ulcer is free from the pancreas.

E. K. M.

NEUROLOGY

Cushing, H. The field defects produced by temporal lobe lesions. *Brain*, 1921, **44**, 341.

This paper ranks in importance, if not in scope, with Cushing's classic monographs on eighth nerve and pituitary tumours. It deals in particular with certain defects of the visual fields which he finds to be the localizing sign of greatest importance in temporal lobe lesions, more especially tumours, and also gives a comprehensive description of the symptom-complex of temporal tumours. Of a series of 663 verified intracranial tumours which have come under Cushing's observation, 276 have been tumours involving the cerebrum proper, and of these 59 have involved the temporal lobe. These form the material upon which the present paper is based.

In an anatomical introduction, Cushing refers to Adolf Meyer's description of 'the peculiar detour of the ventral portion of the geniculo-calcarine path which simulates the existence of an inferior longitudinal fasciculus . . . a portion of the optic radiation, on leaving the geniculate body, plunges far forwards into the temporal lobe to sweep round the horn of the ventricle before it turns backward to end in the calcarine cortex'. There are thus dorso-lateral and ventral bundles in the radiation, of which the latter takes the longer course and extends far forwards into the temporal lobe, to end finally in the anterior and lower part of the visual cortex. Three beautiful diagrams illustrate this anatomical point, and it will be understood that lesions involving the ventral bundle are responsible for defects in the upper quadrants of the visual field. It is interesting to note that this conclusion is in strict accord with Gordon Holmes's observations on the cortical representation of vision (*Medical Science*, 1920, **2**, 65). For the first time the clinical aspect of this anatomical fact is fully described and worked out. In 39 of Cushing's cases of temporal lobe tumour the state of vision and of the patient allowed of a careful perimetric study, and in no less than 33 instances homonymous field defects were found. The commonest defect was a homonymous upper quadrantic hemianopia, often most extensive in the homolateral eye. In the later stages a complete hemianopia was sometimes found.

Heretofore, the so-called 'uncinate attacks' or 'dreamy states', to use the phrase employed by Jackson, their discoverer, have been regarded as the most characteristic focal symptom. However, in Cushing's series, these were present in but 24 cases. Therefore field defects are the most frequent and sometimes the sole localizing symptom in temporal lobe lesions.

Cushing sums up the complete symptom-complex of temporal lobe tumours as follows: (i) The commonest localizing symptom is homonymous quadrantic defects of the visual fields. (ii) The next most frequently observed symptom is the uncinate fit. (iii) In 20 cases generalized convulsions were recorded. A single convulsion without aura was the initial symptom in several cases. In general they were few in number in any given case. (iv) Visual hallucinations were present in 13 cases. They differed from the coloured lights typical of occipital lobe lesions, and were complex pictured scenes referred to that part of the visual field found on examination to be defective. They occurred in association with uncinate

seizures. (v) In 15 cases symptoms suggestive of a cerebellar lesion were noted: nystagmus, vertigo, ataxy of movement, and sub-occipital headache. The presence of the characteristic visual field defects rendered error in diagnosis avoidable. In several cases, also, mention is made in the paper of sixth-nerve paralysis.

It appears that cerebellar and occipital lobe lesions are those most likely to be diagnosed in error when a temporal lobe lesion is actually present, but, as is clear from the above summary, a correct differentiation should be possible.

Cushing concludes that 'perimetry gives us information of paramount diagnostic value, particularly in the early recognition of temporal lobe tumours, the partial field defects short of a hemianopia being especially characteristic of involvement of the optic radiation in this region.'

Like all Cushing's papers, the present one is fully documented and is accompanied by an admirable series of perimeter charts.

F. M. R. W.

Riddoch, G., and **Buzzard, E. Farquhar. Reflex movements and postural reactions in quadriplegia and hemiplegia, with especial reference to those of the upper limb.** *Brain*, 1921, **44**, 397.

In this important and interesting paper the authors carry a step further the physiological analysis of the reflex movements and postural reactions seen in man in disease of the central nervous system. The material upon which their observations and conclusions are based consists of five cases of spastic quadriplegia from high spinal lesions and of cases of hemiplegia. In respect of the lower limbs they break no new ground, but they give a full description and analysis of certain reflex movements of the upper limbs, which, although mentioned by various authors (notably Magnus, *Arch. f. d. ges. Physiol.* 1912, **145**, 455), have never been thoroughly studied. In addition, they discuss at great length the nature of the associated movements familiar in cases of hemiplegia, and, as far as we can follow their argument, appear to draw an important distinction between the processes governing voluntary and reflex movements and those concerned in the production of tonic or postural reactions.

Reflex movements of the upper limb. In spinal quadriplegia the upper limb is spastic in extension and is held adducted and internally rotated at the shoulder, extended at the elbow and wrist, and with the forearm pronated. In these circumstances one or both of two forms of reflex movement can be elicited by appropriate stimulation. The usual response is **the extension reflex of the upper limb**, which consists in retraction, adduction, and internal rotation at the shoulder, extension at the elbow, full pronation at the forearm, with slight flexion at the wrist and extension of the digits. The receptive field for this reaction appears to include the skin and deep structures of the greater part of the reacting limb. The threshold of stimulation appears lowest on the palm, inner aspect of the arm, and in the axilla. Stimulation of the dorsum of the hand is without effect, but the skin over the thorax from third to sixth ribs gives the characteristic response. The form of stimulus essential is one having a harmful or unpleasant character, such as pinching skin or deep structures, or scratching of the skin with a pin. A certain prolongation of stimulation also seems necessary.

In hemiplegia, as is known, the upper limb is spastic in flexion, and in

these circumstances a flexion reflex of the upper limb is obtained from stimuli applied to the same receptive field as that described in the case of the extension reflex. Here, however, the focus of the field is on the palm, and not in the axilla. The response consists in a movement of abduction and external rotation at shoulder and of flexion at all the distal joints. This response was also obtainable, in addition to the extension reflex, from two cases of quadriplegia.

In both instances, there is a tendency to a wide irradiation of muscular reaction to other parts of the body, and the authors trace the direction in which this occurs most freely. In general it may be said that reflex movement of the upper limb is more facile and more ample in the case of quadriplegia than in that of hemiplegia.

Riddoch and Buzzard agree that the associated movements of hemiplegia and quadriplegia are postural reactions such as were briefly described in *Medical Science*, 1922, **5**, 510.

It is in their chapter dealing with the question of reciprocal innervation in movements and in postural reactions that we find it most difficult to follow or agree with the hypothesis of the authors. We gather that they attempt to establish a distinction between the co-ordination of movements on the one hand, and that of postures on the other. This distinction has not been found to obtain in experimental studies, and we believe that Riddoch and Buzzard have misunderstood the facts of clinical observation in suggesting that it exists in man.

In dealing with this complex problem it is essential to be quite clear as to what are the teachings of experimental physiology. As Sherrington has pointed out (*Quart. J. Exper. Physiol.*, 1913, **6**, 251), the conditions under which experimental investigation of reflex co-ordination are carried out are infinitely simpler than any conditions existing in the normal circumstances of life. In the former case we have a single stimulus reaching an animal with its whole musculature quiescent, and in the simple reflex reaction which results there is undoubtedly excitation of the prime movers which carry out the reaction, with reciprocal inhibition of the antagonist muscle groups. Certain other muscles which help to fix the reacting limb in an appropriate position, or to prevent a double and conflicting action of the prime movers when these are double joint muscles, are also excited to contract. These are called synergists. Hence prime movers and synergists are said to be 'identically' innervated, and the antagonists are 'reciprocally' innervated. But it is clear that in normal circumstances a constant inflow of conflicting stimuli reaches the reflex centres, so that each of these is at any given moment under a twofold influence, one element exciting it to discharge and another inhibiting its activity. Out of this seeming disorder it is the function of the nervous system to achieve perfect co-ordination, and this is done by what Sherrington has called 'double reciprocal innervation'. If two stimuli of conflicting character acting upon a reflex centre be very unequal in intensity, the less intense is completely suppressed, but if they be approximately equal the result is an algebraical summation of effect. The prime mover contracts or takes up a posture, but with less force than it would otherwise have done were no inhibitory influence at work, while the antagonists show a lessening of contraction or take up a posture at a greater length of the muscle in proportion to the sum of the two effects. In other words, both members of an antagonist pair are normally in movement or in postural contraction simultaneously.

In this connexion, Sherrington (loc. cit.) says 'it is sometimes assumed that under reciprocal innervation two antagonist muscles necessarily can never be in contraction at the same time . . . this need not be the case . . . Not infrequently the antagonists are concurrently in contraction, and their centres concurrently discharging. What reciprocal innervation does provide is that, in the execution of a muscular act by antagonists, augmentation of contraction or motor discharge shall not occur concurrently in protagonist and antagonist, nor, conversely, decrease of contraction or discharge . . .' In other words, concurrent innervation is equally characteristic of both movement and postural reaction, and further, the term 'reciprocal innervation' is wholly applicable to the processes underlying both. It seems that Riddoch and Buzzard have used the word 'concurrent' as synonymous with 'identical' in this connexion. In this respect and in that of their suggested differentiation between movement and posture we believe that a fallacy has crept into their conclusions. Nevertheless, it is their merit to have drawn attention to the fact that simple reciprocal innervation does not comprehend all the complex muscular acts occurring in the living state, a point somewhat neglected by earlier clinical writers on the subject. Moreover, quite apart from the theoretical considerations it contains, Riddoch and Buzzard's paper describes reflex phenomena of considerable interest, and it may be hoped that the authors will publish elsewhere a more concise account of these for the benefit of those who have not access to the original, or who find its length and complexity too formidable an obstacle to careful study.

F. M. R. W.

Weed, L. H., and **Hughson, W.** (1). **Systemic effects of the intravenous injection of solutions of various concentrations, with especial reference to the cerebrospinal fluid.** *Am. J. Physiol.*, 1921, **58**, 53.

Weed, L. H., and **Hughson, W.** (2). **The cerebrospinal fluid in relation to the bony encasement of the central nervous system as a rigid container.** *Am. J. Physiol.*, 1921, **58**, 85.

Weed, L. H., and **Hughson, W.** (3). **Intracranial venous pressure and cerebrospinal fluid pressure as affected by the intravenous injections of solutions of various concentrations.** *Am. J. Physiol.*, 1921, **58**, 101.

The earlier work of Weed, McKibben, and others on this subject has already been reviewed in *Medical Science*, (1921, **4**, 535). From the experiments recorded in their first paper, Weed and Hughson conclude that the intravenous injection of large amounts of Ringer's solution causes a temporary rise in the cerebrospinal and venous pressures with a rapid return to normal. The arterial pressure is slightly reduced below normal. With a hypotonic solution (distilled water) there is a prolonged increase of the cerebrospinal fluid pressure, and a smaller and more transient increase in the venous pressure. Arterial pressure responds by a slight rise. Strongly hypertonic solutions (30 per cent. salt in Ringer) cause a prolonged and profound fall in cerebrospinal fluid pressure preceded by a sharp initial rise. There is also an initial rise of venous pressure followed by a rapid fall to just below normal. The arterial pressure, on the other hand, after an initial fall, rises to just above the initial pressure. The cerebrospinal fluid pressure is constantly above that in the veins, except after injections of hypertonic solutions. The changes in the cerebrospinal fluid pressure seem in large measure independent of the venous and arterial pressures. (2) Unless the

skull be opened before injection, it is not possible to obtain negative cerebrospinal fluid pressures by injection of hypertonic solutions. Therefore the bony encasement of the central nervous system may be regarded as a rigid container. (3) In the third paper they record observations confirming their view that alterations in the cerebrospinal fluid are largely independent of variations in systemic venous and arterial pressures.

F. M. R. W.

Walshe, F. M. R. On disorders of movement resulting from loss of postural tone, with special reference to cerebellar ataxy. *Brain*, 1921, **44**, 539.

In a recent review in *Medical Science* (1921, **5**, 134) the writer of the paper now under notice drew attention to the fact that the many descriptions and interpretations of the cerebellar symptom-complex to be found in clinical literature were for the most part mutually conflicting and were all empirical and incomplete, and that no final analysis on physiological principles had been formulated. In the present paper such an analysis is attempted, and the conclusion is reached that in loss or impairment of postural tone, as this has been described by Sherrington, is to be found a satisfactory explanation of all the defect symptoms arising from lesions of the cerebellum in man. In other words, atonia is the sole and fundamental cerebellar defect symptom. The term tone is used strictly in the sense defined by Sherrington, namely, as a tonic proprioceptive reflex act, the purpose of which is the maintenance of posture. The experimentally observed results of loss of this tone are described in detail, and their identity with the commonly described symptoms of cerebellar lesions in man indicated. In short, a unit formula for cerebellar ataxy is proposed.

The characters and limitations of the spinal component of tone are described, and the confusion and vagueness of the common clinical conception of tone are indicated as the cause of the complexity and contradiction of the various theories of cerebellar symptomatology and function.

The strikingly different results of cerebellar extirpation in otherwise intact animals on the one hand and in decerebrate preparations on the other are discussed in the light of Magnus's recent work, and it is concluded that, while the cerebellum cannot be said to be an essential centre for proprioceptive tonic reactions, yet it may be the subordinate organ through which the cerebral motor cortex influences postural reactions and co-ordinates these with the various phasic motor activities of the organism.

F. M. R. W.

Turrell, W. J. The principles of electrotherapy and their practical application. *Oxford Medical Publications*, 1922, pp. 276.

Turrell's book is worthy of notice not only on account of its subject-matter, but because it approaches this in a more critical spirit than any text-book on electrotherapy that we have seen. The author refers somewhat bitterly to those who do not accept the claims of electrical methods of treatment, but we think that he is too severe and that the remedy is in the hands of those who practise and teach these methods. Is it surprising if a generation, bewildered by the conflicting and often fantastic theories and by the extravagant claims of electrotherapists, has somewhat illogically jumped to the conclusion that the practical value of electricity as a therapeutic

agent is negligible? We cannot imagine a better remedy for so unfortunate a state of affairs than Turrell's recently published text-book, which stands in a class by itself for its close reasoning and lucidity of expression. It is divided into four main sections, dealing respectively with the action of current electricity, the action of radiant energy, electrodiagnosis, and the application of electrical methods to various conditions of disease. The first section contains a timely and excellent critical review of the theory of ionic medication, which clearly shows upon what unsound foundations this rests. There appears to be no evidence that anything but the most superficial penetration of the skin by drugs is possible. Hence the treatment of such deeply seated conditions as arthritis, sciatica, and the like is quite impracticable. The beneficial results claimed for 'ionization' in these circumstances seem to be due to the effects of passage of the constant current through the tissues, namely, a local rise of temperature and some vasodilatation. The various indications for the use of interrupted currents of low and high frequency and for that of static electricity are clearly stated. In the section dealing with radiant energy, the action of radiant heat, ultraviolet radiation, and X-rays are discussed. In the latter instance the author advances a theory of his own to account for the action of these rays. We are not competent to discuss this, but there are already signs that it does not commend itself to all radiologists. The methods of electrodiagnosis and treatment are clearly described. We think, however, that the pathological details somewhat unnecessarily included in the fourth section might well be omitted, or at least radically revised in a future edition, for they are for the most part neither illuminating nor accurate.

For example, we are told that the essential factor in the treatment of neuritis is the relief of pressure. Either the author's conception of neuritis as a clinical term is something quite unfamiliar to the neurologist, or else he holds original views as to the pathological lesion concerned. In any case, the statement as it stands is quite unintelligible. This, however, is a small fault, seeing that we do not go to a text-book of electrotherapy for our pathology, and in no way detracts from the great practical value of the book. It is a distinct advance on its predecessors, and as such we can recommend it to all who are responsible for the treatment of disease.

F. M. R. W.

Stiefler, G. Die Seborrhoea faciei als ein Symptom der Encephalitis lethargica. [**Seborrhoea faciei as a symptom of lethargic encephalitis.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **73**, 455.

From a study of the literature Stiefler finds that six cases of lethargic encephalitis presenting a Parkinsonian syndrome have been described in which a localized seborrhoeic condition of the face was noted. He records in addition two personally observed cases. The skin of the face was puffy and greasy, and after thorough washing the condition ('Salbengesicht') soon returned. A finger rubbed across the skin becomes greasy and a smear examined microscopically shows the presence of numerous minute fatty particles. The condition develops with the Parkinsonian syndrome and clears up on recovery, when this occurs. Sarbó, who recorded one of the six cases in the literature, discusses the value of the symptom as a localizing symptom referable to the corpus striatum. Stiefler regards it as possibly dependent upon aberration of nervous control over the sebaceous glands, which control

may normally be inhibitory in quality and emanating from the corpus striatum. He identifies it as a seborrhoea faciei. F. M. R. W.

Dreyfuss, H. Multiple Sclerose und Beruf. [**Multiple sclerosis and occupation.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **73**, 479.

Steiner has noted the prevalence, among cases of multiple sclerosis which have come under his observation, of an out-door occupation, and the frequency with which patients of this class claimed to have been bitten by ticks. He has suggested that these animals may act as carriers of the virus, in the same way as the mosquito does in the case of malaria. Stimulated by this observation, Dreyfuss has collected all cases of the disease recorded in the literature since 1900 in which information as to the occupation of the patient has been given. In all, he has found 1,151 cases. From the analysis of this series he finds that country dwellers are far more frequently afflicted than town dwellers, and that, among the former, woodmen, joiners, and carpenters predominate. In the case of the female sex, here also country women predominate. F. M. R. W.

Schuster, J. Ein Fall von multipler Sclerose mit positivem Spirochätenbefund. [**A case of multiple sclerosis, with a positive spirochaete finding.**] *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **73**, 433.

In a clinically diagnosed case of disseminated sclerosis, which proved fatal within a year of onset, Schuster was able to find spirochaetes in no less than six blocks of tissues out of the several hundred he examined. The lesions in which they were observed were fresh lesions, so small as scarcely to be visible to the naked eye. In larger lesions, his observations were uniformly negative. In each case the organism was in the immediate vicinity of a blood-vessel. He concludes that it is only in these minute commencing lesions that we can look with any prospect of discovering the organism. In his case spirochaetes were found in the cerebral cortex and at the margin of cortex and subjacent grey matter. F. M. R. W.

PATHOLOGY

Sabbatani, L. Osservazioni sui globuli rossi trattati col permanganato di potassio. [**Observations on red blood corpuscles treated with potassium permanganate.**] *Haematologica*, 1920, **1**, 485.

Investigations can be carried out by means of suspensions in physiological salt solution of rabbits' erythrocytes and potassium permanganate solutions isotonic with the blood serum of the same animals. When the suspension and the solution are brought in contact, an oxidation takes place in consequence of which the organic colloidal matter contained in the red corpuscles is destroyed and replaced by colloidal manganese dioxide. This is at first in a state of '*sol*', but subsequently passes into one of '*gel*', so that the form of the erythrocytes remains almost unchanged. The colloidal manganese dioxide is brown and forms first in those parts of the corpuscles where the organic matter either is accumulated in greater quantity or is more avid of oxygen. The moment in which the brown colour appears and its

degree of intensity are thus a new means of chemical differentiation of red blood corpuscles and of cells in general. As to the erythrocytes of rabbits in particular, the uniformity of the brown colour assumed by them appears to be against the existence within them both of a differentiated body and of remains of a nucleus. C. d. F.

Zappa, P. La resistenza globulare nelle infezioni sperimentali. [**On globular resistance in experimental infections.**] *Pathologica*, 1921, **13**, 591.

As in the case of haemolytic poisons, the inoculation *in vivo* of haemolytic living germs remarkably increases the globular resistance. The increase is sometimes preceded by a slight diminution. C. d. F.

Bianchini, G., e Gagnoni, R. Le piastrine nel sangue asfittico. [**On platelets in asphyxial blood.**] *Pathologica*, 1921, **13**, 597.

Platelets increase in number in the blood in asphyxia. The increase is progressive from the beginning of the asphyxial symptoms to the death of the animal experimented upon, when their number may even be the quadruple of the average normal one. If the cause of asphyxia is removed and the animal recovers, the increase in the number of platelets (' *piastrinosis* ') disappears within 24 hours. The asphyxial piastrinosis affects the arterial and venous blood in the same way. The multiplication of platelets appears to take place in the asphyxial blood itself. Platelets are seen in asphyxial blood either isolated or arranged in small groups, almost never in large accumulations. Morphologically they do not differ from those seen in normal conditions. C. d. F.

Gamna, C. Ricerche e considerazioni sulla costituzione normale e patologica dei globuli rossi. [**Investigations and considerations on the structure of red blood corpuscles in normal and pathological conditions.**] *Haematologica*, 1920, **1**, 360.

Investigations were carried out by means of the following method: blood films as soon as made are treated with a 0·75 per cent. solution of potassium bichromate to which one adds 0·5 per cent. of acetic acid and 1 or 2 drops of a saturated solution of copper sulphate for every 3 c.cm. of fluid. After 5 to 10 minutes the films are washed in physiological salt solution, stained with eosin, washed and mounted in distilled water.

After this treatment the human normal erythrocytes still have the shape of circular disks; but at one point of their circumference the presence can be detected of a minute, roundish or elongated body or droplet united to each disk by means of a thinner peduncle. The portion of the erythrocytes immediately corresponding to the droplet has a homogeneous aspect and the shape of a biconvex lens. This occupies about one-third of each corpuscle, the remaining two-thirds containing fine granules which diminish in number the nearer they are to the pole of the corpuscle opposite to that from which the droplet hangs. These appearances are due to the action of the reagent upon the fluid haemoglobin contained in the corpuscles, and have been repeatedly described by other authors, and sometimes termed the Maximow phenomenon. But the regularity with which it is obtained in normal conditions enables one to employ the method for investigation into

various forms of anaemia in which, on account of the diminished haemoglobin content, either the phenomenon is not obtained or the hanging droplet, the biconvex zone, and the granules greatly vary in aspect and reciprocal proportions. C. d. F.

Ferrata, A., e Negreiros-Rinaldi. Emoistioblasti e monociti nella milza malarica. [**Haemo-histioblasts and monocytes in the spleen from cases of malaria.**] *Haematologica*, 1920, **1**, 243.

In the malarial spleen 'monocytoid' cells are found similar to the monocytes of the circulating blood. Most of them have a histioid and haemo-histioblastic origin, and come from wandering reticulum and endothelial cells of the spleen itself. These maintain their clasmacytoid aspect and phagocytic property, manifesting itself in the ingestion of malarial parasites and pigment, of erythrocytes and, sometimes, of granulocytes, lymphocytes, and plasma cells. They can, therefore, be spoken of as 'haemo-histioblastic endothelial macrophages'. They give origin, in their turn, to typical monocytes identical with those one finds in the circulating blood from cases of malaria. In course of time they diminish in size and acquire a spherical shape through a process of clasmatolysis. During this transformation their nuclei lose the nucleoli and become somewhat homogeneous and more readily stainable in consequence of the disappearance of some of the chromatic filaments. C. d. F.

Ciaccio, C. Contributo all' istochimica delle sostanze grasse. Sopra un processo per mettere in evidenza gli acidi grassi superiori della serie satura. [**Contribution to the histochemistry of fatty substances. Method for the demonstration of the higher fatty acids of the saturated series.**] *Pathologica*, 1921, **13**, 183.

This method has been in use for some years in Ciaccio's laboratory, but was never published. It is based on the fact that the higher fatty acids of the acetic series form with certain metals, such as Pb, Zn, &c., soaps insoluble in organic solvents. Thus the fatty acids, myristic, palmitic, stearic, oxystearic, and cerebrinic, and their respective soaps, if treated, *in vitro*, with a saturated watery solution of zinc acetate, are no longer dissolved by water, ethyl and methyl alcohol, petroleum ether, benzol, acetone, chloroform, toluol, xylol, and carbon bisulphide, but still have the property of absorbing Sudan III and Scharlach R. On the other hand, the non-saturated fatty acids, such as cholesterin, glycerin, and cholesterin ethers, phosphatides, and cerebrosides, if treated in the same way, remain more or less soluble in the same organic solvents.

For the practical execution of the method, small pieces of tissues are kept for 24 hours in a saturated watery solution of pure zinc acetate. After a quick wash in distilled water, they are passed through the ascending series of alcohols, cleared, and embedded in paraffin. The sections are fixed to slides and treated as usual; they are then stained with Sudan III or scarlet red, counter-stained with haematoxylin, and mounted in gum-syrup or an analogous medium. The fatty acids of the saturated series are coloured orange-red or red according to the stain used. The method gives positive results in cases of fat necrosis, Wallerian degeneration, atheromatous foci, and autolytic processes of adipose tissue. In general it can be used for histochemical purposes in all cases in which the splitting of fat appears

due to the presence of a lipase. There may be, however, two sources of error due to the cerebrosides and fatty pigments (lipo-fuscins). The former are dissolved with difficulty by various organic solvents, and this property is accentuated by the treatment with zinc acetate, so that they may become stained, though faintly, along with the fatty acids of the saturated series. To avoid this, the sections under investigation can be treated, before staining, either with a mixture of methyl alcohol and chloroform, or with ethyl alcohol warmed at 45° C. The lipo-fuscins, which Ciaccio considers as incompletely saturated and oxidized fatty substances, are almost insoluble in organic solvents. To differentiate them from the zinc soaps, sections can be treated, before staining, with a mixture of ethyl alcohol and ether acidified with HCl; all fatty acids are set free by the HCl and become dissolved while the lipo-fuscins are not attacked and, if present, appear afterwards stained electively in the finished specimens. C. d. F.

Gasbarrini, A. Sulla presenza di emoistioblasti e loro derivati nella leucemia linfocitica. [**On the presence of haemo-histioblasts and products of their transformation in the circulating blood in a case of lymphocytic leukaemia.**] *Haematologica*, 1920, **1**, 260.

The author has observed, in a case of acute lymphocytic leukaemia, haemo-histioblasts identical with those described by Ferrata in the circulating blood from cases of chronic granulocytic leukaemia. In addition, transitional forms were seen between such elements and cells considered by the author as lymphoblasts. These can, in his opinion, give origin to prolymphocytes and lastly to lymphocytes. This shows that haemo-histioblasts have a great reproductive capacity and may become transformed into cells of the lymphocytic series. It is not clear, however, how haemo-histioblasts of perivascular origin can pass into the blood-stream. C. d. F.

Bizzarri, A. Anemia grave leucanemica con reperto di mielosi subleucemica e di carcinoma gastrico. [**Case of severe leukanaemia with subleukaemic subacute myelosis and carcinoma of the stomach.**] *Haematologica*, 1920, **1**, 141.

Rare association of a severe form of leukanaemia and gastric carcinoma in the same subject. The blood changes were those of sub-acute anaemia with fall in the haemoglobin percentage and presence of haemocytoblasts, pro-myelocytes, erythroblasts, and megaloblasts. The anatomical leukaemic lesions affected the bone-marrow, spleen, liver, and lymph glands.

C. d. F.

Cattaneo, D. Sulle cellule eosinofile nei processi infiammatori asettici. [**On eosinophile cells in aseptic inflammatory processes.**] *Haematologica*, 1921, **1**, 409.

Pisani, S. Sulla eosinofilia pleurica. [**On pleural eosinophilia.**] *Haematologica*, 1921, **2**, 341.

Cattaneo's investigations were made on inflammatory processes experimentally produced in rabbits by the aseptic introduction into the subcutaneous tissue of different foreign bodies, among which were celloidin tubes closed at one end and filled with red blood corpuscles either of the same or other animals. The author came to the conclusion that the eosinophil cells found

in such inflammatory foci are not locally produced, but originate from the circulating blood. From the way in which the haemoglobin of the erythrocytes introduced into the subcutaneous tissue is eliminated, he, in addition, deduced that there is no relation between local re-absorption of haemoglobin and the production of eosinophil granules.

The observations of Pisani were made on two cases of pleural eosinophilia and some experimental material obtained by injecting some of the pleural effusion from one of his patients into the pleural cavity of guinea-pigs, cats, and dogs. In addition, he injected into the pleural cavity of three young patients affected by a tuberculous exudative pleurisy 10 c.cm. of their own blood. This was defibrinated before being injected, and the pleural effusion first examined in order to ascertain that it was neither haemorrhagic nor eosinophil in character. The histopathological results obtained can be summarized as follows: The pleural effusions investigated were haemorrhagic in character and accompanied by a pericardial eosinophilia; no haemo-eosinophilia was found in either of the two cases examined. The cells imparting to the effusions the eosinophil character were of two sorts: true eosinophils and pseudo-eosinophils. The former prevailed numerically over the latter and could be subdivided into polymorphonuclear eosinophils similar to those of the circulating blood, mononuclear eosinophils of the myelocytic type, mononuclear eosinophils of the pseudo-lymphocytic type. The pseudo-eosinophils were considered as such because of the orange tint of their granules, and could be distinguished in large mononuclear, transitional, and endothelial-like forms. According to the author, the mononuclear eosinophil of the myelocytic type should be considered as the product of an 'abnormal haemo-cytoblastic or haemo-histioblastic reaction', while the pseudo-eosinophil appeared due to 'a special granular degeneration' of the erythrocytes ingested by various phagocytic cells. The results obtained from the experiments in animals were in favour of this opinion, though the simple addition of defibrinated blood to the non-haemorrhagic pleural effusions of human beings was insufficient to impart to them either an eosinophil or a pseudo-eosinophil character. C. d. F.

Zamorani, M. Vasto ematoma intrasplenico in un caso di leucemia ad emocitoblasti. [**Large intrasplenic haematoma in a case of haemocytoblastic leukaemia.**] *Haematologica*, 1921, **2**, 427.

Case of chronic myelogenous leukaemia which in course of time had taken a distinct haemocytoblastic (myeloblastic) character. At the post-mortem examination a very large haematoma and smaller haemorrhagic nodules were noticed in the spleen. The blood-cyst and haemorrhagic foci appeared connected with various causes such as venous congestion due to small but numerous thromboses; areas of necrosis diminishing the resistance of the wall of blood-vessels; new production of blood-capillaries and blood-spaces; but chiefly a congenital predisposition, which could not, however, be well determined. The case is interesting because of the rarity of haematomata in cases of leukaemia in general, and with localization in the spleen in particular, this being, perhaps, the first observations of the kind.
C. d. F.

Morpurgo, B. (1). Sur quelques relations biologiques entre deux rats unis par greffe siamoise. [**On some biological relations between rats joined by Siamese lateral grafting.**] *Ann. de med.*, 1920, **8**, 1.

Morpurgo, B. (2). Consequenze della nefrectomia nei topi siamesi disuguali. [**Consequences of nephrectomy in mice of different size joined by Siamese lateral grafting.**] *Atti d. r. Acc. Lincei di Roma*, 1921, **30**, 13.

If two rats in every respect alike are joined together by Siamese lateral grafting (lateral coeliostomy), they can live together for many months without any appreciable alteration of their metabolism. The quantities of food and drink taken, of urine excreted, of nitrogen assimilated, of nitrogen and salts eliminated, are about the same for each of the two animals. If one of the two is weaker or smaller than the other, they live together only for a time, even if they belong to the same race, family, and litter. Generally the smaller one soon dies, and is found in a remarkable state of general atrophy similar to that one sees after protracted and total starvation. All through the period of the progressive atrophy the weaker animal eats less than its companion, drinks very much, and excretes very little urine. Death is preceded by a short period of pallor, fall of temperature, and apathy, ending in drowsiness and coma. The stronger animal eats a great deal, drinks very little, and excretes much more urine than even a normal rat. The urine of the stronger animal is more dilute than that of the weaker, but it also contains greater quantities of nitrogen and salts. All these various phenomena develop and progress at the same time, so that it is impossible to say which of them is the primary one, but they all point to a trouble chiefly consisting in a flow of water from the weaker animal towards the stronger one. This, however, is not sufficient to explain the progressive atrophy of the smaller animal, because the natural supposition that nutritive material is carried with the water from the one animal to the other does not appear to be the case, for other experiments by the same author have proved that during the starvation of one or the other of the two animals there is only a minimal transference of nutriment between the two organisms.

With the object of further investigating the continuous flow of water taking place from the weaker towards the stronger of two rats or mice of different size joined by lateral coeliostomy the author thought of having resort to nephrectomy. This was carried out in one or the other or both twins of series of Siamese pairs. The results obtained are: After bilateral nephrectomy of the weaker mouse or rat, the compensation of the renal function is effectuated through the kidneys, or even one kidney of the stronger one. But bilateral nephrectomy of this last is not sufficient to stop the flow of water towards it. After bilateral nephrectomy in one animal and monolateral in the other, the renal function is carried out in a sort of labile condition and a small increase in the amount of work effectuated by the remaining kidney, such as that subsequent to a change of diet, is enough to cause the picture of a renal insufficiency. This constantly manifests itself in the mouse totally deprived of the kidneys and is extremely like human uraemia, but entirely differs from the pathological condition seen in single animals after bilateral nephrectomy.

C. d. F.

Viale, G. Ricerche elettrofisiologiche. I. Le polarità delle correnti elettriche consecutive alle lesioni nei girini. II. Il decremento delle correnti di riposo e delle correnti di demarcazione nei muscoli. [**Electro-physiological investigations. I. Polarity of electric currents after lesions in tadpoles. II. Decrement of rest and demarcation currents in muscles.**] *Arch. di Fisiol.*, 1921, **19**, 243, 249.

The following conclusions are interesting also from a pathological point of view: (1) The electric currents derivable from altered embryonic tissues are only a manifestation of the general law according to which altered tissues are, in well-preserved conditions of vascularization and innervation, electrically positive. This agrees with the opinion formerly expressed by the author and Hertlitzka that the inner portion of the cells is likewise electrically positive. (2) The living muscle is always electrically positive in opposition to the tendon which is negative. After death the muscle is negative while the tendon is positive. C. d. F.

Camis, M. Ricerche chimico-fisiche sull' emoglobina con particolare riguardo alla dottrina dell' aggregazione molecolare. [**Chemico-physical investigations on haemoglobin, with special reference to the theory of molecular aggregation.**] *Haematologica*, 1921, **2**, 149; *Arch. di sc. biol.*, 1921, **2**, 134.

(1) The surface tension of dialysed solutions of haemoglobin (Hb.) at concentrations varying between 0·4 and 19·2 per cent. is smaller than that of distilled water. Such tension diminishes as the temperature is raised from 10° C. upwards; it grows as the concentration of the Hb. solution is increased up to a certain limit, beyond which it diminishes as the concentration is increased. The surface (molecular) energy follows a similar curve; its maximum corresponds to a concentration of about 6 per cent. For concentrations oscillating between 0·4 and 6 per cent. such a curve has a parabolic character probably due to phenomena of superficial absorption. The addition of 0·006 up to 0·1 per cent. of lactic acid to solutions of Hb. or of laked blood diminishes their superficial tension. This shows that a molecular aggregation has taken place in the solution. The addition of lactic acid to solutions of Hb. or of haemolysed blood diminishes their coefficient of luminous extinction, which indicates a diminution in the number of particles pierced by the rays of light. The effect of the addition of lactic acid is more pronounced in the case of solutions of Hb. than in that of solutions of blood. These results show that in cases of acidosis due to lactic acid the Hb. molecules collect in larger groups than in normal conditions. (2) The doctrine of the molecular concentration of Hb. holds good also as regards the normal influence upon erythrocytes of electrolytes, which appear to cause an arrangement of the blood-pigment into small molecular groups. The influence of lactic acid upon the molecular aggregation of Hb. is a reversible phenomenon. C. d. F.

Chistoni, A. Ricerche sulla reazione attuale del siero di sangue. I. Modificazioni della reazione attuale del siero di sangue provocata dal salasso. [**Investigations on the actual reaction of blood serum. I. Modifications of the reaction caused by blood-letting.**] *Haematologica*, 1921, **2**, 213.

Conclusions: (1) after blood-letting the concentration of the H-ions of blood-serum is increased if the subtraction of blood is such as to lower the blood-pressure and therefore cause the passage of lymph into the

blood-stream ; (2) the serum of the lymph from the thoracic duct is more alkaline than the blood-serum. Its reaction does not change during an experimental lymphorrhea ; (3) an increase in the concentration of the H-ions of the blood-serum may be obtained by preventing the passage of lymph into the venous blood for a certain time ; (4) the changes caused in the reaction of blood-serum by blood-letting last in small dogs from a few to a maximum of six hours, at which time the reaction is again normal. C. d. F.

Baggio, G. (1). Le modificazioni anatomiche della milza consecutive a tiroidectomia. [**Changes of spleen after thyroidectomy.**] *Arch. di Fisiol.*, 1921, **19**, 89.

Baggio, G. (2). Le modificazioni anatomiche della milza consecutive a stimizzazione. [**Changes of spleen after extirpation of thymus.**] *Ibid.*, 1921, **19**, 299.

Experiments were made on rabbits. When removing the thyroid care was taken not to injure the external parathyroids, which were left *in situ*. After extirpation of the thyroid the spleen showed a considerable diminution in size and weight but no histological changes. This atrophy of the spleen appeared connected with a cachectic condition affecting the whole organism. After extirpation of the thymus the weight of the spleen was found diminished in 78 per cent. of all cases. The average diminution was of 182 mgm. In 62·50 per cent. of all animals experimented upon a diminution of the body-weight was noticed. A diminution in the weight of the spleen and the body at the same time was found in 60 per cent. of all cases. As after thyroidectomy, no histological changes could be detected in the atrophying spleens. C. d. F.

Haneborg, A. O. ***The effects of alcohol upon digestion in the stomach.*** (Printed as a supplement to *Acta Med. Scand.*) 1921, pp. 123.

Haneborg's work from the Physiological Laboratory of the Christiania University is a study of the reaction of the stomach to alcohol in health and disease, of the fate of alcohol in the system, and of germane subjects. With regard to the increased secretion of gastric juice caused by small doses of alcohol (15 c.cm. of '*aquavit.*' with food), this effect was not obtained till the alcohol had been absorbed. It seemed most likely that this increased secretion was due to the generally exciting action of the alcohol on the nervous system. Alcohol was found to have no effect upon the proteolytic action of gastric juice *in vitro* when the concentration of alcohol did not exceed 10 per cent. Above this dilution it reduced the proteolytic action to about one-half of normal, and in a dilution of 20 per cent. it prevented all proteolysis *in vitro*, doubtless on account of precipitation of pepsin by the alcohol. Comparatively large doses of alcohol (50 c.cm. of *aquavit.*) given after a meal had a constant effect in promoting secretion, whereas the same dose on an empty stomach disturbed digestion to a considerable extent. Within the first 3 to 4 hours of ingestion, 80 to 90 per cent. of the alcohol had undergone combustion, which was practically complete after another two hours. It was also found that only 0·1 per cent. and up to 0·5 per cent. of the ingested alcohol was excreted by the kidneys. Alcohol given by the mouth was absorbed chiefly by the stomach, and only to a slight extent by the intestines.

Turning from physiological to pathological conditions, Haneborg quotes experiments to show that chronic gastritis does not appear to prevent the absorption of alcohol by the stomach. The effect of alcohol on patients suffering from hyperacid dyspepsia and gastric ulcer was an increase in the quantity of HCl and the total acidity, with increased pyrosis and pain. In cancer of the stomach, however, alcohol seemed to relieve pain, nausea, and a sense of distension, although it did not affect the secretion of gastric juice. Digestion was promoted by small quantities of alcohol in gastric achylia and chronic gastritis, and in several cases alcohol yielded free HCl in a gastric juice where it had previously been lacking. But when achylia was complete, alcohol had no secretory effect. Though small doses of alcohol (15 c.cm. of '*aquavit.*') taken with food promoted digestion in healthy persons, the effect of these small doses under pathological conditions proved to be largely dependent on individual peculiarities. This was probably so because, in the last instance, alcohol acts through the nervous system, the receptivity and reactive capacity of which vary considerably.

Haneborg concludes that his investigations have given a blow, a conditional blow, to the 'ancient reputation of alcohol as a stomachicum'. An incidental discovery, made in the course of his investigations, was the remarkable frequency with which apparently healthy persons over the age of 50 show a deficiency of free HCl. It was either absent or considerably reduced in quantity in 50 per cent. of the persons over this age. These persons will, as a rule, experience no digestive troubles as far as the stomach is concerned, provided their food is suitably composed and prepared. But as soon as these conditions are no longer fulfilled, troubles arise which in certain cases may be allayed by alcohol, provided it does not constitute more than 10 per cent. of the total contents of the stomach.

C. L.

Hill, L., and **McQueen, J.** **Capillary blood-pressure and the glomerular filtration theory.** *Brit. J. Exper. Pathol.*, 1921, **2**, 205.

The paper deals with the modern theory of the secretion of urine, and evidence is brought forward to show that pressure in the glomerular capillaries is a low one, and that physiological permeation—not filtration—controls the passage of fluid through the glomeruli. Observations on the circulation in the frog's glomeruli are detailed and support these conclusions, which are also borne out by experiments of Hamburger, which demonstrate the selective action of the epithelium covering the glomeruli.

P. F.

BACTERIOLOGY

Topley, W. W. C., Weir, H. B., and **Wilson, G. S.** **The interrelationships between the various members of the *B. enteritidis B. paratyphosus* B group of bacteria.** *J. Hyg.*, 1921, **20**, 227.

In experimental epidemics among mice, initiated by feeding with cultures of *B. enteritidis* (Gärtner), a varying proportion of the animals, which succumb yield cultures of an organism having serological characters

which bring it into close relationship with *B. aertrycke* (Mutton), and differentiate it sharply from *B. enteritidis*. The lesions observed in large numbers of mice differ in no way, according as one type of organism or the other is the infecting agent. The importance of determining whether the two infections are to be regarded as distinct entities, or as together forming a homogeneous outbreak of disease, suggests the necessity for further inquiry into their mutual relationship.

It is shown, from consideration of the mortality-chart of a long-continued epizootic, that the deaths referable to infection with each of these organisms, in successive waves of enteric infection in mice, are arranged in such a way that it is impossible to separate off individual waves referable to each infection, and each having their own maximal and minimal points. Consideration of another chart, referring to an epizootic in which infection due to the aertrycke type of bacillus co-existed with infection due to a mouse-pasteurella, shows that in this case successive waves of each infection may be traced, each having well-defined and separable maxima and minima.

These facts are considered in the light of our knowledge of other infective diseases, caused by bacterial species which may be differentiated into separate serological types; and it is suggested that there are many similarities between these experimental results and certain observations which been made in outbreaks of meningococcal and pneumococcal infection in man.

Observation of many successive generations of individual strains, both of the Gärtner and the aertrycke type of bacillus, has shown that it is a common occurrence for a strain, on first isolation, to be agglutinated by sera specific for each of these types, while later it becomes inagglutinable by one of them. In other instances the change has occurred in the reverse direction. In either case it has always been possible to determine the true serological type of the strain by testing successive subcultures, or by absorption. No evidence has been obtained that one type can arise from the other by mutation.

The more important organisms belonging to this large group are briefly described, and their interrelationships are considered in the light of the above facts. It is suggested that many of them, which have hitherto received separate specific names, should rather be regarded as forming serological races of one bacterial species, analogous to the races or types of meningococci or pneumococci. It is further suggested that the specific name of *B. enteritidis* should be employed for this group, with the addition of a name denoting the variety or type to which a given strain belongs, where such differentiation appears to be justifiable and desirable.

W. W. C. T.

Franceschelli, D. Ricerche biologiche sul bacillo tubercolare e sui suoi prodotti. I. L'azione dei fermenti della digestione sul bacillo di Koch e sui suoi prodotti. [**Biological investigations on tubercle bacilli and their products. I. Action of gastric ferments on Koch's bacillus and its products.**] *Riforma Med.*, 1921, **37**, 914.

Tuberculin is completely destroyed by pepsin and trypsin, the action of which is more rapid if used together. This shows that tuberculin is a toxalbumin and the futility of administering tuberculin *per os*. The wax and fat of tubercle bacilli are not attacked by the pancreas lipase, hence the

conclusion that Koch's bacillus cannot be destroyed in the intestine by such a ferment alone. The fact that the protecting envelope of Koch's bacillus is not destroyed by fat-splitting ferments explains why after having been submitted to their action it still maintains its staining properties. The nuclein isolated from Koch's bacillus possesses the chemical characteristics of all nucleins, but it is not affected by trypsin. C. d. F.

Sanfelice, F. Intorno alla trasformazione dei bacilli acido-resistenti in bacilli della tubercolosi. [**On the transformation of acid-fast bacilli into tubercle bacilli.**] *Ann. d'ig.*, 1921, **31**, 457.

The author has already shown (*Medical Science*, 1921, **4**, 452; *Boll. Ist. Sieroter. Milanese*, 1920, **1**, 337; 1921, **2**, 1) that acid-fast bacilli isolated from tuberculous animals may become transformed into tubercle bacilli and thus change their morphological and biological properties. These results have been recently confirmed by Kolle, Schlossberger, and Pfannenstiel (*Arb. a. d. Inst. f. exper. Ther.*, 1921, referred to by the author). The importance of such observations for the aetiology of human tuberculosis has induced Sanfelice to make a new set of experiments, the results of which are summarized by him approximately as follows: (1) Acid-fast bacilli, in passing through the animal organism, may become transformed from saprophytic into parasitic bacilli, morphologically, culturally, and pathogenetically identical with tubercle bacilli. (2) Acid-fast bacilli after having acquired parasitic features adapt themselves to the life-conditions of the new host. But in passing from species to species they may lose their pathogenic power and acquire vaccinating properties. This transformation is due to a reaction on the part of the host. Very likely tubercle bacilli in passing through the animal organism are in part transformed into non-pathogenic acid-fast varieties. (4) From organisms affected by tuberculosis, together with tubercle bacilli, pseudo-tubercle acid-fast bacilli are also spread into the surroundings. Tuberculous infection is probably transmitted not only through tubercle bacilli but also through acid-fast germs which re-acquire their pathogenic power in infected organisms. C. d. F.

Vagliano, M. S. Des réactions leucocytaires consécutives à l'inoculation des bacilles tuberculeux. [**Leucocytic reactions following injection of tubercle bacilli.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 1130.

This is a study of the leucocytic reactions in rabbits, obtained by the inoculation, intravenously or otherwise, of human and bovine tubercle bacilli, living or dead, sensitized or non-sensitized. In the first days after inoculation of dead non-sensitized T.B. a definite leucocytosis occurs and may persist for 30 to 40 days. With living non-sensitized bacilli there is also a leucocytosis reaching a plateau in 10 to 20 days and after marked oscillations descending to the normal line in 2 to 3 months. With sensitized killed bacilli no change was found in the leucocytic curve, while with sensitized living bacilli there was a progressive leucocytosis after a normal interval of 40 days. In both groups there was an initial leucopenia for the first 24 hours following the inoculation. With regard to the variations in the differential counts the author found that after inoculation of dead bacilli (sensitized or not) there was first a diminution in the number of mononuclear cells, which, however, gradually reappear and cross the normal line between the 9th and 12th day, the complement-fixing reaction making its first

appearance on the latter date. After inoculation of living bacilli, sensitized or not, the mononuclears show oscillations of great magnitude and irregularity. Eosinophils are unaffected but basophil cells were always increased—a fact which may be of some importance. Injection of tuberculin made from egg cultures of T.B. was without effect on the leucocytes. W. B.

Baldwin, E. R., and Gardner, L. U. Reinfection in tuberculosis. Experimental arrested tuberculosis and subsequent infections. [**B.**] *Am. Rev. Tuberc.*, 1921, **5**, 429–517.

Baldwin and Gardner have carried out a long series of investigations in guinea-pigs in order to determine the importance of the frequency of infection in the provocation of tuberculosis. The guinea-pigs were primarily infected by inhalation of human tubercle bacilli of low virulence, such as those cultivated by Trudeau in 1891. With attenuated cultures from this parent stock, an attempt was made to produce completely arrested tuberculosis before the results of reinfection were studied. A few animals ultimately developed chronic generalized tuberculosis as a result of this primary infection, but most escaped without lesions extending beyond the lungs and tracheo-bronchial glands. The exceptions were probably the outcome of an accidental mixture with a virulent strain of bacilli. After describing their technique and discussing the numerous pitfalls in such a line of research, Baldwin and Gardner review their findings and point out that they seem to indicate that reinfections *may* be solely exogenous, and that, when relatively large doses are given by inhalation, exogenous reinfection is perfectly feasible. But, while both primary and secondary tuberculous infections by inhalation follow the same course in the tissues of the animal, the second infection does not form caseated tubercles with the same regularity seen in primary tuberculosis. Instead, a localized inflammatory reaction, with a moderate degree of proliferation without caseation, is the rule. The tracheo-bronchial glands suffer no further disease in the mild reinfections; in other words, an abortive form of the disease follows. The exceptions to this rule can be explained either by overdosage or by absence of primary infection. Baldwin and Gardner's paper includes a clinical and epidemiological study of the problem of reinfection. Their survey of the literature shows how amazingly nebulous and contradictory are the views of clinicians and epidemiologists on this point. C. L.

Racchiusa, S. Sui granuli metacromatici del bacillo difterico. Ricerche microchimiche. [**On metachromatic granules of *B. diphtheriae*. Microchemical investigations.**] *Ann. d'ig.*, 1921, **31**, 545.

For the demonstration of the polar or metachromatic granules of *B. diphtheriae* the following two methods are recommended because of their simplicity: (1) Stain films for 10 to 20 minutes in a 1:1,000 solution of thionin; differentiate in alcohol or in water acidulated with acetic acid. The granules are stained violet-red, the bacillary bodies pale blue. (2) Stain for 10 to 15 minutes in Giemsa's solution diluted in the usual way; differentiate in acetone or acidulated water. The granules are violet-blue, the bacilli pink. In addition to these two methods, many others were tried by the author, who came to the conclusion that the metachromatic granules of *B. diphtheriae* are formed of a substance similar to, if not identical with, mucin. C. d. F.

Bell, A. S. G. The serological differentiation of some strains of *Bacillus diphtheriae*. *J. Roy. Army Med. Corps*, 1922, **38**, 48.

The author has studied the agglutination reactions in a series of 130 strains of *B. diphtheriae*, all of which gave fermentation in glucose and maltose but not in saccharose. The Park-Williams No. 8 strain of *B. diphtheriae* was first injected into a rabbit and all the strains of diphtheria bacilli were tested with the serum obtained. From the strains which failed to agglutinate, selections were made at random and injected into other rabbits, and in this way several sera were obtained. Three strains were finally selected, and it was found that the sera obtained agglutinated 80 per cent. of the 130 strains of diphtheria bacillus. In type I the number was 13 per cent., in type II 6 per cent., and in type III 61 per cent. In spite of agglutinogenic differences all the strains tested seemed to produce the same toxin and antitoxin. Diphtheria-like bacilli which fermented saccharose all failed to show any agglutination with any of the diphtheria agglutinating sera. The technique of preparing and testing the agglutinating sera is given. W. B.

Papacostas, G., et **Gaté, J.** A propos de l'antagonisme entre le bacille diphtérique et le pneumobacille. Son explication par le rôle empêchant de la toxine pneumobacillaire vis-à-vis de la sécrétion de la toxine diphtérique. [**On the antagonism between *B. diphtheriae* and *Pneumobacillus*. Explanation—the inhibiting property of pneumobacillus toxin upon diphtheria toxin.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 1038.

It is believed that the association of the bacillus of Friedländer with *B. diphtheriae* renders infections more benign. The authors have studied this question in animal experiment. The filtrate of cultures of Friedländer's bacillus does not neutralize diphtheria toxin *in vivo* or *in vitro*. By growing the two cultures together and comparing the action with cultures of *B. diphtheriae* alone the authors believe that the ability of the latter to form toxin is inhibited to a certain extent, and the amount of growth is lessened. This is not altogether due to the changes in reaction of the medium induced by Friedländer's bacillus. W. B.

Haythorn, S. R., and **Lacy, G. R. Virulent *Treponema pallidum* recovered from a still-born infant after twenty-six hours.** *J. Infect. Dis.*, 1921, **29**, 386.

In this paper are recorded the results of inoculation experiments with serum from the cutaneous blebs and from the lungs of a seven-month still-born syphilitic infant.

A post-mortem examination was carried out 26 hours after the infant had been delivered, the body and placenta being kept over-night in the refrigerator. The case showed the usual signs of congenital syphilis to be well marked. Numerous samples of *Treponema pallidum* were demonstrable both by dark-ground and by staining methods. Serum from the blebs and from crushed lung, in both of which great numbers of typical treponemas could be seen, was inoculated into the testicles of two rabbits. Indurated nodules appeared in both cases, from which treponemas were recovered. Repeated transfers have been carried out over a period of nine months.

The authors state that a belief is prevalent that *Treponema pallidum* loses its virulence almost as soon as the host is dead. They conclude from

this case and from other experiments not recorded that the treponema may retain its virulence for a period between 24 and 36 hours after the death of the host. G. T. W.

Brown, W. H., and **Pearce, Louisa** (1). **Experimental production of clinical types of syphilis in the rabbit.** *Arch. Derm. & Syph.*, 1921, **3**, 254–62.

Brown, W. H., and **Pearce, Louisa** (2). **Experimental syphilis in the rabbit.** *J. Exper. M.*, 1920, **31**, 709–64: 1920, **32**, 473–512: 1921, **33**, 495–514, 518–38; 1921, **34**, 167–84.

Eberson, F. (1). **Immunity studies in experimental syphilis. Infectivity and survival of *Spirochaeta pallida* in rabbits, with observations on some strains from latent syphilis.** *Arch. Derm. & Syph.*, 1921, **3**, 775–87.

Eberson, F. (2). **Dissemination of *Spirochaeta pallida* in experimental syphilis.** *Arch. Derm. & Syph.*, 1921, **3**, 111–16.

Lacy, S. R., and **Haythorn, S. R. Viability of *Spirochaeta pallida* in excised tissue and autopsy material.** *Ann. J. Syph.*, 1921, **5**, 401–8.

Some interesting work on experimental syphilis in the rabbit has been carried out recently by Brown and Pearce. The animals were inoculated either in the testicle or scrotum with two strains of *S. pallida*, which had been carried in rabbits for several years. All results were positive. The incubation period was from two to six weeks in testicular, and from one to two weeks in scrotal, inoculation. The lesions pursued a cyclic or relapsing course, and the spirochaetes showed periodic changes in activity corresponding to the periodic changes in the lesions, similar to those which occur in other spirochaetal infections, such as relapsing fever. The inoculation lesions in the scrotum were of two types: (1) a circumscribed indurated granuloma resembling human chancre; (2) a diffuse infiltration more resembling human secondary syphilides. The regional lymphatic glands were always affected. The lesions underwent spontaneous resolution in the course of a few weeks or months.

As a rule syphilis in the rabbit is limited to the initial lesion, but Brown and Pearce found that under certain conditions generalized syphilis, analogous to human syphilis, could be produced. They found that the resistance to general infection by the *S. pallida* depended to a great extent on the degree of reaction at the site of inoculation, and that any condition which tended to inhibit the reaction without affecting the infecting organisms favoured general infection. For instance, unilateral instead of bilateral inoculation, castration, to shift the defensive mechanism to other tissues and the use of therapeutic agents capable of inducing resolution of the primary lesion, without destroying the infecting organisms, was found to alter the course of infection and lead to generalization. By such means generalized syphilis was induced in 200 rabbits. From the results of their experiments Brown and Pearce conclude that: (1) The occurrence of generalized syphilitis in the rabbit depends chiefly on the protective reaction at the site of the primary lesion, and to a less extent on the relative susceptibility of other tissues. (2) This protection may not affect all tissues at the same time and at the same rate, but may be progressive from the primary lesion to successive groups of tissues, so that one tissue is protected while another is not. (3) According to this conception, the

tissues involved represent a measure of the progress and effectiveness of the reaction in the animal, which is indicated by groups of tissues becoming affected in a given order; the bones first, then the skin, and lastly the eye (in the rabbit). (4) By early and radical interference (castration) it is possible to alter the course of the disease so that bone lesions supplant the testicular lesions in the defensive reaction; conversely, by permitting the testicular reaction to progress to a certain point (late castration) it is possible to confer protection on the bony tissues, in which case no bone lesions occur and general infection begins in the next groups of tissues, the cutaneous and ocular. (5) In the majority of animals inoculation in both testicles produced a high degree of protection, but sometimes failed to protect the ocular tissues, which then showed the only signs of general infection. (6) From the manner in which the infection responded to modifications in the defensive reaction it would appear that wide variations in the clinical types of syphilis may be due to this one group of causes; but this does not exclude biological variations in *S. pallida* as another possible cause. For their experiments Brown and Pearce used one given strain of *S. pallida*.

The clinical types of generalized syphilis produced in the rabbit, although not identical with those of human syphilis, were sufficiently analogous for comparison, and included lesions of the periosteum and bones, lesions of the skin and its appendages, including local and general alopecia, onychia, and paronychia, macular, papular, and granulomatous syphilides, lesions of the buccal, genital, and anal mucous membranes, and ocular lesions, including keratitis. Rabbit syphilis differs from human syphilis in that the bones are affected before the skin and mucous membranes. [See also *Medical Science*, 1921, **5**, 349.]

Eberson, having previously demonstrated that syphilis in man, while outwardly inactive, may harbour active spirochaetes in the lymphatic glands and semen (*Medical Science*, 1921, **5**, 18), has studied the infectivity and survival of *S. pallida* in rabbits. He found first that the infectivity is not diminished when the spirochaetes are taken from old syphilitic lesions. The survival of *S. pallida* in experimental syphilis was subject to considerable variations and bore no relation to the incubation period, the age of the lesions, or the number of animal passages. The organism was found in conditions of latency with no lesions; for example, inoculated testicles which remained negative for indefinite periods and showed no lesions were found to harbour spirochaetes capable of infecting other animals. Certain strains of *S. pallida*, especially those isolated from latent sources in man and rabbit, had a tendency to produce latency in the inoculated animals.

Eberson has also studied the dissemination of *S. pallida* in rabbit syphilis. He found the organism in the blood and in the regional lymphatic glands as early as seven days after inoculation, some days before any sign of primary lesion appeared. He regards this early dissemination as opposed to any life-cycle of the organism during the incubation period of syphilis.

Lacy and Haythorn have experimented with a view to determine the viability of the *Spirochaeta pallida* in dead tissues. This was decided by the presence of motility and the results of experimental inoculation. Material was taken from the tissues of an infant which died of congenital syphilis, from excised chancres, and the serum from chancres. Some

material was kept at room temperature, some in a refrigerator at 2° to 4° C. As regards motility, this was observed in human autopsy material up to 48 hours after death, the body being kept in a refrigerator; in chancres for seven days after excision; in serum from chancres, kept in sealed capillary tubes at room temperature, for 121 days; in saline suspension of rabbit's testicle under the same conditions, and also in refrigerator, for 58 days. Inoculation of rabbit's testicle was positive with syphilitic autopsy material 26 hours after death; with chancre, 24 hours after excision; with emulsified syphilitic rabbit's testicle after 24 hours. When material was completely dried all results were negative. From these experiments the authors conclude: (1) That spirochaetes kept in serum or moist tissue, either human or animal, may retain slight motility for upwards of three months. (2) That reliable dark-ground examinations can be made on tissues or fluids collected several hours previously, provided they are kept moist and cool. (3) Spirochaetes may remain virulent in autopsy material for 26 hours or longer. (4) Complete drying is probably fatal to the *Spirochaeta pallida*. C. F. M.

Kolmer, J. A., and **Lucke, B.** (1). **A study of the histologic changes produced experimentally in rabbits by arsphenamin.** *Arch. Derm. & Syph.*, 1921, **3**, 482–514.

Kolmer, J. A., and **Lucke, B.** (2). **A study of the histologic changes produced experimentally in rabbits by neo-arsphenamin.** *Arch. Derm. & Syph.*, 1921, **3**, 515–30.

Kolmer, J. A., and **Lucke, B.** (3). **A study of the histologic changes produced experimentally in rabbits by mercurial compounds.** *Arch. Derm. & Syph.*, 1921, **3**, 531–70.

Schamberg, J. F. Clinical commentary on studies of histologic changes in organs induced by arsphenamin, by neo-arsphenamin, and by mercury. *Arch. Derm. & Syph.*, 1921, **3**, 571–8.

Kolmer and Lucke have studied the histological changes produced by arsphenamine, neo-arsphenamine, and mercury in the rabbit. They found that large doses of arsphenamine (12 gm. per 60 kilos) produced severe vascular changes, consisting of congestion and thrombosis; also degenerative changes, chiefly in the liver, suprarenals, and spleen. These changes were much more severe with an acid solution than with an alkaline solution or with disodium arsphenamine. Repeated small doses of 0·6 gm. per 60 kilos body-weight, however, produced only slight histological changes, which were probably not severe enough to interfere with function. The changes produced by neo-arsphenamine were less severe. Mercury, administered in the form of soluble or insoluble injections, by inunction, or by the mouth, in maximum human doses, caused tissue changes in all the organs. These changes were most apparent in the kidney, in the form of tubular or glomerular nephritis, and in the brain, in the form of perivascular round-celled infiltration.

Schamberg, in a commentary on the above researches, draws attention to the predilection of arsenical compounds for the blood-vessels, liver, and suprarenals, and of mercury for the kidneys and brain. Mercurial nephritis has long been known, but that mercury may cause cerebral changes appears to be new to us. He attributes the greater frequency of jaundice and acute yellow atrophy since salvarsan was introduced to deficient elimination of

arsenic caused by mercurial affection of the kidneys. For this reason, he advises that mercury and arsphenamine should not be administered simultaneously but in separate courses, mercury being preferably given after arsphenamine. He mentions that in 12,000 injections of arsphenamine given at his clinic, without the addition of mercurial treatment, jaundice was only observed three times and exfoliating dermatitis twice. C. F. M.

Eberson, F. Immunity studies in experimental syphilis. Spirocheticidal properties of serums in latent and experimental syphilis, with some observations on immunity. *Arch. Derm. & Syph.*, 1921, **4**, 490–511.

Eberson experimented with sera taken from subjects known to have latent syphilis, with a history of both old and recent infection, free from visible symptoms, and mostly untreated; also from inoculated rabbits. A combined *in vitro* and *in vivo* method was used to determine the spirochaeticidal activity of the serums by mixing 2 c.cm. of serum with 0·1 c.cm. of a virulent suspension of *S. pallida*. This mixture was inoculated into the testicles of normal rabbits after incubation at 37° C. for one and a half hours. Normal human and rabbit sera were used as controls. The rabbits injected with normal serum developed lesions after 4 or 5 weeks, while those injected with spirochaeticidal serum remained negative, as confirmed both by subsequent microscopic examination and subinoculation. The results of these experiments showed that the serum in latent syphilis has spirochaeticidal properties when symptoms are absent, but when the infection is active or recent, this protective property is absent. Hence it would appear that a true immunity exists at some time in the course of syphilitic infection. According to Eberson, latency signifies that a balance has been struck between the antibodies and the spirochaetes, and the latter are at this period innocuous for the host. That immunity need not imply a condition incompatible with the life of the parasite is shown in the case of trypanosome and spirillum infections, and the carrier state of such diseases as typhoid and malaria. Eberson concludes that in syphilis there is a progressively increasing immunity of the tissues with corresponding formation of antibodies, commencing as a local immunity reaction with the initial lesion and extending from one group of tissues to another. In favour of this view he cites the work of Brown and Pearce on the production of clinical types of syphilis in the rabbit (*vide supra*). According to Eberson, the generally accepted view that failure to reinoculate with syphilis means existing disease rather than a state of immunity requires modification. The presence of *S. pallida*, he remarks, in the tissues appears to co-exist with immunity to reinfection, in the same way as in piroplasmosis and trypanosome disease. The presence in the body of *S. pallida*, virulent for a new soil, need not imply disease, but rather a latent stage in which the spirochaetes survive in the immunized body. Failure to reinfect with syphilis may mean the entry of spirochaetes into surroundings which favour their lodgement without setting up visible manifestations. Eberson's results also showed that a negative Wassermann reaction following antisyphilitic treatment may or may not correspond to spirochaeticidal activity in the serum; also that continued treatment which renders this reaction negative does not appear to nullify the protective property of the serum. He suggests the possibility of the serum from latent syphilis having a therapeutic value. C. F. M.

Sartori, C. Sull' inoculazione endocerebrale del vaccino. [**On intracerebral inoculation of vaccine.**] *Pathologica*, 1921, **13**, 490.

The present paper is a confirmation of the results obtained by A. Marie (*Compt. rend. Soc. de biol.*, 1920, **83**, 476), and Levaditi, Harvier, and Nicolau (*ibid.*, 1921, **85**, 345) by the intracerebral inoculation of vaccine pulp into rabbits. Sartori has reached the following conclusions: (1) a purification of the vaccine virus is possible by inoculating it intracerebrally into rabbits; (2) not all samples of vaccine pulp appear to have the same affinity for the nervous centre; (3) the vaccine virus, when active for nervous centres, causes in them lesions of an inflammatory character (diffuse meningo-encephalitis); (4) the virus does not spread from the nervous centres to other organs; (5) the cerebral virus can be transplanted into the testis and *vice versa*.

C. d. F.

Sani, L. Sull' isolamento dei tripanosomi del sangue. [**On the isolation of trypanosomes from the blood.**] *Ann. d'ig.*, 1921, **31**, 536.

The blood of an infected dog is collected directly from the heart into a flask containing physiological salt solution to which 1·5 per cent. of sodium citrate has been previously added. The quantity of the salt solution must be about the same as that of the blood one intends to collect. Immediately afterwards, the mixture of citrated salt solution and blood is centrifuged at a low speed (700 turns per minute). In this way the bulk of red corpuscles collects at the bottom of the centrifuge tubes while the leucocytes and most of the trypanosomes remain in the supernatant fluid. This is poured into other tubes and centrifuged at the maximum speed available. The deposit at the bottom of the tubes now contains many trypanosomes mixed with leucocytes and some erythrocytes. The fluid is discarded and the deposit first diluted with saline in the proportion of 1 : 20 and then mixed with complement and specific haemolytic serum of a titre previously established. The mixture is kept for 20 minutes at 37° C. in a water-bath and centrifuged once more. At the bottom of the tubes only living trypanosomes are found. In order to obtain some more trypanosomes, the mass of erythrocytes separated at the beginning may be diluted with salt solution, mixed with complement and specific haemolytic serum, and kept for one hour at 37° C., during which it is frequently and vigorously shaken. The flasks containing the mixture are now allowed to stand for a little while, when the upper fluid can be poured off and the trypanosomes, collected at the bottom of the flasks, washed with saline, and added to those previously obtained. The method appears to work quite satisfactorily and to compensate for the trouble of first preparing the specific haemolytic serum.

C. d. F.

Mühlens, P., u. **Kirschbaum, W.** Parasitologische und klinische Beobachtungen bei künstlichen Malaria- und Recurrensübertragungen. [**Parasitological and clinical observations in artificial transference of malaria and relapsing fever.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 1.

During the last few years Wagner von Jauregg has advised the production of an artificial febrile infection in the treatment of general paralysis of the insane, and has reported favourable results with this method of treatment. Doerr and Kirschner (1921) reported some results in which an infection was induced by malarial parasites. The present authors have carried

out a large number of experiments in which general paralytics were inoculated with tertian, quartan, or tropical malarial blood, or blood containing *Spirochaeta duttoni*. Sixty-two patients received tertian blood, 5 quartan, and 9 tropical, while 12 received blood from recurrent fever. In general the injury to the patient was trivial. All the parasites were propagated in many generations. For instance, a table is given to illustrate the transference of tertian parasites through no fewer than 20 generations without any change of form or type. In the case of the induced tertian fever the incubation period varied between 5 and 29 days, in quartan 15–30 days, in tropical fever 7–14 days, and in the case of spirochaetal fever 3–8 days. In general the experimental was milder in course than the naturally acquired disease. The tertian cases reacted best to quinine although a 'quinine-fast' strain was not proved with certainty. The doses of malarial blood employed were 0·5 to 1·0 c.cm. subcutaneously of defibrinated blood. Indigenous specimens of *Anopheles maculipennis* (from Cuxhaven) allowed to suck the blood of a patient with crescents showed a development up to the sporozoit stage at 23–25° C. in January. Any action that the induced malarial attacks had on the patients was slight and indirect so far as concerns their paralytic symptoms and lesions. W. B.

Bussalai, L. Sopra un caso di favo scutulare delle parti glabre da *Achorion quinckeanum*. [**Case of favus of the hairless skin due to *Achorion quinckeanum*.**] *Pathologica*, 1921, **13**, 473.

Reference has been already made to a case of favus of the hairless skin due to *A. quinckeanum* (see Truffi, M., *Medical Science*, 1922, **5**, 437). Bussalai now describes a quite similar case observed in a boy of 12 years of age, to whom the disease was apparently transmitted from mice, which were very numerous in the house where he lived, and some of which had been seen running on his bed. C. d. F.

Sangiorgi, G. Di un reperto '*Rickettsia prowazeki*' nel sangue di un dermotifoso. [**The occurrence of '*Rickettsia prowazeki*' in the blood of a typhus patient.**] *Pathologica*, 1921, **13**, 450.

The author has observed typical and numerous *Rickettsia prowazeki* in films made from the blood of a typhus patient and stained with Giemsa's fluid in the usual way. The author emphasizes the fact that the blood was taken from a place in which the typhus rash was quite plainly recognizable and immediately after its appearance. How it is that such typical and easily obtained pictures have not, as yet, been seen by other authors Sangiorgi cannot explain. The paper is illustrated with two microphotographs evidently spoiled by reproduction on paper of unsuitable quality. C. d. F.

Volpino, G., e Graziadei, G. Reperti microscopici nell' encefalite letargica. [**Microscopic findings in lethargic encephalitis.**] *Ann. d'ig.*, 1921, **31**, 533.

Reference has already been made to the observations of Volpino and Desderi (*Medical Science*, 1921, **4**, 452, and **5**, 148), as to the presence of amyloid-like bodies in the brain substance from cases of lethargic encephalitis. Volpino and Graziadei now point out that the bodies previously described, though similar to corpora amylacea, differ from them in certain

respects. For instance, they sometimes show a central acidophil part which in ordinary amyloid bodies is generally basophil. At any rate they propose calling these corpora amylacea 'bodies of type A' in order to distinguish them from others termed 'bodies of type B'. These were recently observed in the white substance from the basal nuclei of an acute case of the disease. The bodies of type B are characterized by their irregular form and size, and by a granular content which may be stained with Ziehl's fuchsin solution. C. d. F.

BIOCHEMISTRY

Hess, A. F., Unger, L. J., and **Pappenheimer, A. M. Experimental rickets. The prevention of rickets in rats by exposure to sunlight.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **19**, 8.

Shipley, P. G., Park, E. A., Powers, G. F., McCollum, E. V., and **Simmonds, N. The prevention of the development of rickets in rats by sunlight.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **19**, 43.

Hess and his co-workers have sought to correlate the observations previously made of the beneficial effect of sunlight on rickets in children and in experimental animals with the finding of Howland and Cramer that the phosphorus content of the serum of rachitic children rises to normal when they are given cod-liver oil.

Infants suffering from rickets were placed in direct sunlight for periods of half an hour to several hours. The rachitic signs diminished or disappeared and the general condition improved. The tables show a rise in the inorganic phosphorus, which was originally below 3·5 mgm. per 100 c.cm. blood and rose to 4 mgm. The authors believe that the experiments establish a definite chemical basis for heliotherapy. They also furnish the first definite evidence of metabolic change in the animal body due to solar rays.

The experimental contribution of McCollum and his colleagues is concerned with the effect of sunlight on a series of rats, six of which were kept in a well-lighted laboratory in Baltimore and twelve were sent to New Haven and exposed to sunlight. During the periods, which lasted sixty-two and sixty-seven days, the solarized animals were exposed to the direct rays. The total amount of exposure varied between two hundred and forty-two and two hundred and seventy-three hours. The diets of the two sets of animals were the same. The control rats kept in the Baltimore laboratory had all the gross and microscopic evidences of rickets. The rats exposed to sunlight showed no signs of rachitic deformation. Though sunshine completely prevented rickets it did not entirely compensate for the deficiency of phosphorus in the diet either as regards growth and development of the rat as a whole or of the skeleton. The effect of sunlight appears to be exactly analogous to what was obtained by Howland and Park by feeding cod-liver oil. Neither sunlight nor cod-liver oil meets the defects in the composition of the diet by supplying to the body either calcium or phosphorus, but meets them indirectly by so raising the potential of cellular activity as to secure the most efficient utilization of those substances available in the body which are directly or indirectly concerned with ossification and calcification. C. G. L. W.

Kolmer, W., u. **Scheminzky, F.** Ernährungsversuche an Kaulquappen und die Bedeutung des Tryptophans. [**Feeding experiments on tadpoles, and the importance of tryptophane.**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 93.

Tadpoles were fed on various diets known to be more or less deficient in tryptophane, and the lengths of time they survived were compared. The experiments showed that tryptophane is an indispensable amino-acid for these, as for higher, animals. C. L. E.

Eddy, W. H., Heft, H. L., Stevenson, H. C., and **Johnson, R. Studies in the vitamin content. II. The yeast test as a measure of vitamin B.** *J. Biol. Chem.*, 1921, **47**, 249.

Search for the nature of the vitamin substances still goes on. It will be remembered that a new and simple test had been proposed by Williams and others for testing the presence of vitamin B in an extract. This consisted in finding out whether the growth of yeast was stimulated by it or not. It was further suggested that vitamin B was identical with the so-called bios factor, which Pasteur originally found necessary for the development of yeast in artificial media. Since the publication of Williams's work, considerable doubt has been cast upon the test, it being apparent that other factors besides the vitamin could stimulate the growth of yeast cells. In this paper a careful study of various factors has been made. It has been found that the concentration in which the stimulating factor is given matters considerably. In low concentrations there is a stimulating effect, which may, however, be converted into the reverse when added in high concentration. It also appears that other factors than the vitamin may act as stimulants. This being the case, the yeast test has, to a large extent, lost its practical utility at the moment, though the search for the factors which stimulate growth is bound to lead to results of general importance. R. A. P.

Alvarez, W. C., and **Mahoney, L. J. Action currents in stomach and intestine.** *Am. J. Physiol.*, 1922, **58**, 494.

Instruments have been devised by means of which the action currents of the digestive tracts can be studied. Numerous records obtained from animals are given. A striking result is that large currents can be obtained from stomachs and bowels, which, to the naked eye, show no peristaltic movement. Splanchnic stimuli which inhibit the contractions of the bowel have little or no effect on the rhythmic action current. The author compares this curious condition, indicating the presence of rhythmic chemical processes which are not necessarily transformed into mechanical processes, with an 'automobile with the engine running and the clutch out. From time to time some mechanism lets the clutch in and motion appears.' The stomach shows a negative variation travelling every 12–30 seconds from the cardiac region to the pylorus. Occasionally, the pace-maker shifts, even to the pyloric region. The arrival of gastric waves at the pylorus is followed by marked electrical changes in the duodenum.

Records were obtained also from the gall-bladder, liver, common bile-duct, and caecum. W. C.

Wheelon, H. Relation of the gastric content to the secretory and motor functions of the stomach. *Arch. Int. Med.*, 1921, **28**, 613.

A study of 296 gastric samples obtained from 64 normal medical students by (*a*) complete tube evacuation at the end of one hour after the test meal; (*b*) the 'fractional' method; (*c*) removal of 10 c.cm. samples in rapid succession one hour after the test meal. The author concludes that the acid concentration is not usually constant in all parts of the stomach at the end of one hour; the withdrawal of the stomach contents for the purpose of determining the acid concentration, the type of the meal, the position of the top of the tube, and duodenal regurgitation are factors which militate against the acceptance of fractional curves as indicative of the secretory functions of the stomach. O. L. V. de W.

Müller, H. Bestehen Unterschiede in der Pepsinverdauung des Frosches und der Warmblüter? [**Is peptic digestion identical in frog and mammal?**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 214.

The conditions of activity of pepsin prepared by extracting the mucosa of the frog's stomach, were compared with those for mammalian pepsin solutions. The conditions were identical, both as regards the relation between activity and enzyme concentration, and the effect of temperature on the velocity of the action. C. L. E.

Isaac Krieger, K. Zur quantitativen Bestimmung der Fermente in Duodenalsaft. [**Quantitative estimation of ferments in duodenal contents.**] *Ztschr. f. klin. Med.*, 1921, **92**, 259.

Observations on lipase, diastase, and trypsin. Considerable variations occur in the amount of these ferments present in the duodenal contents of normal individuals. Each ferment may vary independently. In cases of achylia gastrica the pancreatic ferments are secreted normally, and this was also the case in the diabetic patients examined. The author states that the method of examination employed is useful in testing pancreatic function, but gives no definite evidence of this in his tables. O. L. V. de W.

Dodds, E. C., and Bennett, I. T. II. Variations in alveolar carbon dioxide pressure in relation to meals; a further study. *J. Physiol.*, 1921, **55**, 381.

Dodds has already shown that a rise of 2–6 mm. occurs in the alveolar CO_2 pressure in the first half to three-quarters of an hour following a meal, and that the rise is succeeded by a fall to below the original level. The experiments were designed to throw light on that portion of the CO_2 curve which falls below the normal level. Oatmeal gruel introduced into the duodenum by means of the Einhorn tube produced an immediate fall in the alveolar CO_2 pressure. Water produces the same result. The result is the same whether the gruel is faintly alkaline or acid. The fall in alveolar CO_2 is believed to be the result of secretion of alkali in the intestine, the most important source of this alkali being the pancreatic juice.

Gastric lavage with a weak solution of atropine produces an immediate fall in the alveolar CO_2, and no rise occurs as the result of a test meal. Local application of atropine to the duodenal mucosa raises the fasting CO_2 level, and in cases thus treated a test meal still produces a rise in the alveolar CO_2 pressure, but no fall below the fasting level is seen when the food enters the duodenum. O. L. V. de W.

Eweyk, C. van, u. Tennenbaum, M. Sekretinstudien, I, II. [**Secretin studies.**] *Biochem. Ztschr.*, 1921, **126**, 238.

Protein (casein) materials, after heating to 150–70° C., become secretin-containing, in the sense that they will cause the secretion of gastric juice in the Pawlow dog. This effect is due to the presence of histamine. It had been shown previously by Popielski that histamine would act as this type of secretin. The hormone from spinach is not histamine. R. A. P.

Loewi, O. Über humorale Übertragbarkeit der Herznervenwirkung, II. [**Humoral transmission of cardiac nerve effects.**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 201.

The contents of the saline-fed frog's heart, if collected during the stimulation of the vago-sympathetic, and administered to a second perfused heart, produce in it the effects which the nerve-stimulation caused in the first. These effects may be either an inhibition, an acceleration, or first one and then the other. Occasionally, however, especially in toads, the contents from an inhibited heart have an accelerating effect on the second heart. Whatever the substance causing inhibition may be, it is certainly not choline. The accelerating substance is not present in the ash of perfusates containing it. C. L. E.

Wiggers, C. J., and **Katz, L. IV. The contour of the ventricular volume curves under different conditions.** *Am. J. Physiol.*, 1922, **58**, 439.

Continuation of previous work (see *Medical Science*, 1921, **5**, 270). The rate of ejection during the phase of 'maximum ejection' is uniform. It is suddenly much reduced during the phase of 'reduced ejection'. In diastole there is at first a rapid inflow which accounts for 30 to 50 per cent. of the total filling. Then the inflow is retarded and 'diastasis' supervenes. This phase of diastasis is always distinct when the cycle is of sufficient length.

When the venous pressure is increased by saline infusion the ventricles respond with increasing strokes. The resulting increase in systolic discharge is associated with an increase in diastolic volume, an increased length of systole, and also an increased intraventricular pressure. The statement that the only constant factor determining discharge is a change in systolic length cannot be regarded as demonstrated.

Increased arterial resistance reduces the duration of systole and does not prolong it, as previous workers have stated. In order to maintain a normal systolic discharge the velocity of ejection is increased in a heart in good condition. When the increase in arterial pressure is accompanied by an increased venous pressure the two factors act in an opposite sense on the duration of systole and there may then be a prolonged duration of systole.

The effects of vagus stimulation, of asphyxia, and of adrenalin are also discussed. W. C.

Kritschewsky, J. L. Über die Wirkung des Salvarsans auf das Serum von Tieren und auf die Formelemente des Blutes *in vitro*. [**On the effect of salvarsan upon the serum of animals and upon the formed elements of the blood *in vitro*.**] *Biochem. Ztschr.*, 1921, **126**, 11.

Salvarsan will precipitate colloids. It has also the property of agglutinating animal blood corpuscles in high dilutions. For alkaline

solution, this is of the order of 0·00002 per cent., and half of this amount for acid solution. Salvarsan will haemolyse erythrocytes, but seems to require different concentrations for the corpuscles of different animals. These various actions of salvarsan can be antagonized by addition of serum.

The results are taken to explain in part the symptoms of death from salvarsan observed in animals. These symptoms are supposed to be connected with the disturbance of colloidal complexes, in the blood.

R. A. P.

Rothlin, E. Über den Einfluss von Corpus luteum-Extrakt auf die Erythropoese bei künstlich anämisierten Kaninchen. [**The effect of corpus luteum extract on erythropoesis in rabbits rendered anaemic by artificial means.**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 102.

Secondary anaemia was produced by bleeding the rabbits, and the influence of corpus luteum extracts, administered *per os* or by subcutaneous injection, on the regeneration of the red corpuscles was investigated. No noticeable effect was found. C. L. E.

Lehmann, J. Über die Hemmungswirkung der Barium-, Strontium- und Calciumchloride bei der Blutgerinnung. [**On the inhibitory action of barium, strontium, and calcium chlorides in blood coagulation.**] *Skandin. Arch. f. Physiol.*, 1922, **42**, 35.

The addition of calcium, strontium, or barium chloride to normal blood does not shorten the coagulation of blood, but inhibits it. W. C.

Foster, D. P., and **Whipple, G. H. Blood fibrin studies. I. An accurate method for the quantitative analysis of blood fibrin in small amounts of blood. II. Normal fibrin values and the influence of diet. III. Fibrin values influenced by transfusion, haemorrhage, plasma depletion, and blood-pressure changes. IV. Fibrin values influenced by cell injury, inflammation, intoxication, liver injury, and the Eck fistula.** *Am. J. Physiol.*, 1922, **58**, 365, 379, 393, 407.

The authors have determined the fibrin content of blood in dogs and in man by a new method in a great variety of conditions as indicated in the titles. Considerable fluctuations due to a variety of stimuli were observed. Diet substances may be concerned in these fluctuations. Tissue injury and inflammation exert a powerful stimulus upon fibrinogen production. Small doses of liver poisons (chloroform, phosphorus, and hydrazine) have a stimulating effect, large doses are depressing. A number of other conditions have been studied and the general conclusion is drawn that there is a constant manufacture and utilization of fibrinogen in the body and that the liver is probably the only potential source of fibrinogen in the body. Since exclusion of the liver by an Eck fistula or injury of the liver by chloroform is associated with a delayed healing of a sterile abscess, it is suggested that fibrinogen or other substances manufactured in the liver play a part in normal wound healing. W. C.

Gram, H. C. A new method for the determination of the fibrin percentage in blood and plasma. *J. Biol. Chem.*, 1921, **49**, 279.

A method is here described in which the fibrin content of blood can be estimated with a considerable degree of accuracy upon 4·5 c.cm. of blood.

Simultaneous determinations of the cell volume, the platelets, and of the coagulation time are also included. A few observations upon the amount of fibrin in the blood of normal and diseased persons are given. Men seem to have less fibrin than women. The variations in men are from 0·19–0·11 per cent. in the blood of the normal individual. They are probably constant for the individual. In anaemia the percentage for blood is high and in polycythaemia is low. R. A. P.

Adair, G. S., Barcroft, J., and **Bock, A. V. The identity of the haemoglobin of human beings.** *J. Physiol.*, 1921, **55**, 332.

Samples of haemoglobin from different individuals freed from corpuscles give oxygen dissociation curves which are indistinguishable. Preparations made by slow dialysis of the blood against distilled water may simulate solutions in appearance, but, containing intact though swollen corpuscles, give dissociation curves far different from those of true aqueous solutions of haemoglobin. O. L. V. de W.

Killian, J. A., and **Kust, L. Significant chemical changes in the blood co-incident with malignant tumours.** *Arch. Int. Med.*, 1921, **28**, 813.

A study of the urea, uric acid, creatinin, non-protein nitrogen, sugar, and CO_2 combining power of the blood in 119 cases of malignant neoplasms. Of these patients 80 per cent. showed an increase of the uric acid content of the blood, and 60 per cent. an increase in urea nitrogen and creatinin. The authors attribute this finding to a more or less severe impairment of kidney function, since the relative retention of the different bodies resembled that seen in renal disease, and since in the patients showing such retention phenolsulphonephthalein excretion was also impaired. The occasional hyperglycaemia observed (by Myers's method) they also attribute to defective renal function. In many of the cases showing nitrogen retention the CO_2 combining power of the blood was also diminished. O. L. V. de W.

Cohn, E. A. Über das Verhalten des Reststickstoffs im Blute bei Grippe. [**Non-protein nitrogen of the blood in influenza.**] *Ztschr. f. klin. Med.*, 1921, **92**, 201.

The author, in the investigation of 150 cases of influenza, found that the non-protein nitrogen of the blood exceeded 45 mgm. per 100 c.cm. in 30 per cent. He attributes this increase in the non-protein nitrogen content to increased protein catabolism, the result of the infection, and excludes renal damage, or increased blood concentration as possible causes.
O. L. V. de W.

Haggard, H. W. The fate of sulphides in the blood. *J. Biol. Chem.*, 1921, **49**, 519.

The inhalation of H_2S does not lead to sulph-haemoglobinuria. This can only be produced when haemoglobin is already completely reduced, and, on the whole, is formed with difficulty. The plasma is able to oxidize H_2S to harmless substances, which combine with the sodium of the plasma. H_2S does not form sodium sulphide in the plasma. In the process of this oxidation, oxygen is withdrawn from the corpuscles. This seems to be the

cause of the toxic effect of large quantities of the gas. It is claimed that sodium sulphide when given intravenously is very rapidly oxidized by the blood, in a comparatively short period. R. A. P.

Bloor, W. R. Lipaemia. *J. Biol. Chem.*, 1921, **49**, 201.

The presence of abnormal fat in the blood in diabetics cannot fail to be of interest to the clinician. Whereas the normal individual has a matter of 0·5 gm. of lipoid present in 100 c.cm. of plasma, the diabetic may have as large an amount as 4·35 gm. This paper is a continuation of previous work by the same author. He confirms the work of Horiuchi upon rabbits, in which animals a relatively heavy lipaemia is induced by bleeding, showing that the same changes cannot be induced in the normal dog. Where persistent lipaemia is present, it is found that there is increase in amount of cholesterol and lecithin as well as in fat proper. The greatest increase occurs in the fat and the next greatest in the cholesterol. As a rule fat increases in amount first, followed by lecithin and then cholesterol. The lipaemia clears up in the reverse order. The increase in blood lipoid may come either from the fat depôts or from the food. In a general discussion, it is concluded that the cause of the lipaemia lies in a disturbance of the balance between the inflow and the outflow of fat in the blood. Three cases of diabetes have been studied. In one of them the breaking of diet, by eating large amounts of milk and cream, led to the appearance in the blood of an amount of lipoid fourteen times above the average value for normal men. Diacetic acid appeared in the urine in this case. It is believed that the origin of the lipaemia in the haemorrhagic rabbit and the diabetic is different. In the rabbit, it is a question of an abnormally large inflow of fat into the blood, the condition can be induced in the absence of food. In the diabetic, on the other hand, there is an inhibition of the normal mechanism of outflow of fat from the blood. This view leads to the suggestion that there may be a hormone responsible for the fat control, as well as the carbohydrate control, both being partially or completely in abeyance in the diabetic. R. A. P.

Blatherwick, N. R. Observations on blood fat in diabetes. *J. Biol. Chem.*, 1921, **49**, 193.

These experiments were designed to test the diabetic diet of Newburgh and Marsh. The latter suggested as a new diet for diabetics a low protein, low carbohydrate, and high fat diet. They claimed that there was no increase in the amount of acetone bodies, as perhaps might be expected upon the basis of the increased fat. It was shown that the amount of fat in the blood remains remarkably constant in diabetic individuals, with increasing amount of fat in the diet. There is further no appearance of acetone bodies in the urine. The indication is, therefore, that at any rate over short periods fats may be used. It is as yet uncertain whether a continuance of the high fat diet may not lead to bad effects. R. A. P.

Lifschütz, I. Die Abbauprodukte des Cholesterins in den tierischen Organen. (Begleitstoffe des Blutcholesterins.) [**Decomposition products of cholesterin in animal organs. (Substances accompanying cholesterin in the blood.)**] *Ztschr. f. physiol. Chem.*, 1921, **117**, 201.

The cholesterin fraction of blood fat contains not only cholesterin but also derivatives which are probably oxidation products of cholesterin. They fall into two classes, one of which gives double compounds with digitonin, while the other does not. H. W. D.

Hubbard, R. S. 1. Note on the determination of β-hydroxybutyric acid. Determination of the acetone bodies in the urine. 2. Determination of the acetone bodies in blood.

Hubbard R. S., and **Wright, F. R. 3. Blood acetone bodies after the injection of small amounts of adrenalin chloride.** *J. Biol. Chem.*, 1921, **49**, 351.

Improvement of technique is bound to throw light upon the more obscure problems connected with carbohydrate and fat metabolism. The method described in these papers requires half an hour for the oxidation, the final determination being an iodometric titration. The amount of acetone bodies in normal urine was found to be low, in agreement with other observers, about 2 mgm. per 100 c.cm. Of this the acetone from the β-hydroxybutyric acid was more than that from the acetone plus aceto-acetic acid. The induction of acetonuria in a normal subject by the ingestion of an excessive fat diet showed, in addition to the normal increase in the amount of acetone, a change in the relative proportion of the acetone from β-hydroxybutyric acid and from acetone plus aceto-acetic acid. The latter increased before the former. It is suggested that this indicates that 'the substance which finally fails to be completely burned under the conditions studied is aceto-acetic acid rather than β-hydroxybutyric acid'. Other possibilities are, however, considered. A study of the blood shows that the acetone from the normal blood is between 0·1–1·0 mgm. per cent. from all three acetone bodies. There is, however, no normal relation between the proportion of the acetone bodies, except that in diabetics the acetone from β-hydroxybutyric acid is in excess. The administration of adrenalin as a rule caused a significant rise in the amount of acetone bodies in the blood. R. A. P.

PeténYi, Beza, u. **Lax, H.** Über die Wirkung des Adrenalins auf den Blutzucker. [**On the effect of adrenalin upon the blood-sugar.**] *Biochem. Ztschr.*, 1921, **126**, 272.

It is claimed, as the results of experiments upon children, that the hyperglycaemia occurring after subcutaneous injection of adrenalin is followed by a hypoglycaemia. In cases of tetany the blood-sugar value is not so constant as the normal. In these cases, also, the hyperglycaemia after adrenalin is not so marked, whereas the hypoglycaemia is mostly deeper and of longer duration. R. A. P.

Vogel, R., u. **Bornstein, A.** Über ein paradoxes Verhalten des Zuckerstoffwechsels bei gleichzeitiger Einwirkung von Pilocarpin und Adrenalin. [**On a paradoxical behaviour of the sugar metabolism to the simultaneous action of pilocarpine and adrenalin.**] *Biochem. Ztschr.*, 1921, **126**, 56.

Adrenalin and pilocarpine when injected separately into dogs cause a raising of the blood-sugar percentage. The simultaneous injection of

these substances leads to no change in the blood-sugar. This is considered to be evidence of a difference in the mechanism of the production glycaemia in the two cases. R. A. P.

Van Slyke, D. D., and **Stadie, W. C. The determination of the gases of the blood.** *J. Biol. Chem.*, 1921, **49**, 1.

An improved type of apparatus for the determination of the gases of the blood is described, together with several details of improved technique. A simple shaker is also described for use with the Van Slyke blood-gas apparatus. R. A. P.

Stewart, G. N. Researches on the circulation time and on the influences which affect it. V. The circulation time of the spleen, kidney, intestine, heart (coronary circulation) and retina, with some further observations on the time of the lesser circulation. *Am. J. Physiol.*, 1921, **58**, 278.

The following figures were obtained for the circulation time:

Organs.	*Species.*	*Time in Seconds.*
Spleen	Cat	4–5
Kidney	Rabbit	6–8
Intestine	Dog, rabbit	2·5–4
Testis	Rabbit	4
„	Dog	7
Coronary circulation	Dog, rabbit	2–3
Retina	Rabbit	2

W. C.

Greenthal, R. M., and **O'Donnell, W. S. Studies on the fragility of the red blood cells.** *Am. J. Physiol.*, 1921, **58**, 271.

The fragility of human erythrocytes was tested against saline solutions of decreasing concentrations. The majority of normal bloods show beginning haemolysis at 0·425 per cent. and complete haemolysis at 0·325 per cent. The fragility is increased after treatment with CO_2 gas and hypertonic saline. It is decreased after treatment with sodium bicarbonate solution and arsenic (Fowler's solution). CO gas, adrenalin, atropine, diphtheria, and tetanus toxins, and ether anaesthesia produced no change.

In cases of cardiac disease with cyanosis the fragility of the red blood cells is increased.

These observations and the work of Van Slyke and Cullen on the effect of passing CO_2 and O_2 through the blood explain why the blood-cells of venous blood are more fragile than those of arterial blood. W. C.

Ellinger, P. Die Beeinflussung der Oxydationsgeschwindigkeit von roten Blutkörperchen durch Kalium und Radioaktivität. [**The influence of potassium and of radio-activity on the rate of oxygen usage in red blood corpuscles.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 266.

The presence of potassium is essential for the respiration of blood-cells. Potassium can be replaced by rubidium but not by caesium. Radio-active substances cannot replace potassium, and indeed injure the respiratory process. Fluorescein behaves similarly, but very small amounts of eosin increase the oxygen usage. H. W. D.

Wagner, R., und **Parnas, J. K.** Über eine eigenartige Störung des Kohlenhydratstoffwechsels und ihre Beziehungen zum Diabetes mellitus. Eine klinisch-experimentelle Studie. [**A peculiar disturbance of carbohydrate metabolism and its relation to diabetes.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 361.

The authors have investigated a case of glycosuria in a girl of 8½ years who had been under observation since the age of 4. The principal physical sign was a greatly enlarged liver. On examination of the urine it was found that the morning urine gave an intense reaction for acetone compounds. With the administration of both starch and sugar there was a glycosuria. The remarkable feature of the case was that, on examination of the blood, it was found that during fasting the fluid was entirely free from sugar. After food, an extreme hyperglycaemia took place. In the fasting stage injections of adrenalin did not produce the hyperglycaemia which occurs in normal subjects under similar conditions. Hence the disturbance is not due to a mobilization of glycogen, but is due to a lack of mobilizable carbohydrate. In this case the administration of protein, lactates, glycerine, and amino-acids after fasting raised the content of sugar in the blood. Thyroid in fairly large doses was without effect; with larger doses lipaemia, lipuria, and steatorrhoea occurred. During one day the normal quota of sugar appeared in the blood.

The authors look upon the case as one of azooamylia, i. e. a lack of function on the part of the liver to store up sugar in the form of glycogen. On the other hand the regulating mechanism is absent which in the normal fasting subject catabolizes protein in order to keep the sugar content of the blood at its normal level, and in cases of diabetes leads, in spite of the absence of carbohydrates in the food, to a hyperglycaemia. This process, however, can be replaced by the administration of thyroid, and thus shows the importance of this gland for sugar metabolism in that the thyroid regulates the endogenous protein metabolism and prepares this protein for the formation of sugar.

In the relation of pancreas and thyroid, the latter acts as a brake to excessive pancreatic activity. It is difficult in the present case to make out clearly the relations of pancreas, liver, and thyroid. It is possible that with the dysfunction of the liver there is an independent disturbance of the thyroid which leads to an inhibition of endogenous protein breakdown; or the lack of liver function and activity of the thyroid are determined by a disturbance of the pancreas. C. G. L. W.

Straub, H., und **Meier, K.** Die Alkalireserve der Nierenkranken. [**The alkali reserve in kidney diseases.**] *Biochem. Ztschr.*, 1921, **124**, 259.

The paper contains a large number of observations upon the CO_2 capacity at different CO_2 tensions of the bloods of various patients with kidney disease. In general it is found that there is a disturbance of the normal acid-base equilibrium in the body, leading as a rule to a depletion of the alkali reserve—a condition referred to as hypocapnia. In five of the kidney cases, the contrary condition of hypercapnia, i. e. raised CO_2 combining capacity was found.

The cases where either normal CO_2 capacity or hypercapnia are found tend to be associated with a dyspnoea, showing periodic breathing. It is suggested that there is a change in the activity of the respiratory centre in these cases. The grade of abnormality does not run parallel with the increase in the amount of the Rest N in the blood. R. A. P.

Fiske, C. H. Observations on the alkaline tide after meals. Inorganic phosphate and acid excretion during the post-absorptive period. *J. Biol. Chem.*, 1921, **49**, 171.

Observations upon the reaction of the urine after a meal show that the urine becomes, quite suddenly, more alkaline in the second or third hour after the meal. This is especially marked in the case where the meal has been a large one. In the case of a small one, it is difficult to be certain whether any change is not merely a return to normal conditions from the previous meal. The author does not seem to regard it as by any means conclusively established that the alkaline tide is due to the secretion of the gastric juice. The maximum alkalinity after a protein meal is reached at a time when the excretion of phosphate and sulphate is at a maximum—that is, when sulphuric acid is being produced in the body.

In the paper upon phosphate excretion, it was found that there occurs a large increase in the phosphate output. This is at its maximum in the middle of the afternoon. The rise takes place gradually from the drop which occurs during the night. There tended to be oscillations in the curves, probably associated with the meals. The drop in phosphate seems to correspond most nearly with the titratable acidity. It is considered that the prevailing view that phosphate excreted represents the amount of acids requiring neutralization in the body is not correct. The general curve of phosphate excretion is not altered by giving sodium bicarbonate. The partial explanation put forward is that there is an active retention of phosphoric acid in the morning which is released later on in the day.

R. A. P.

Fricke, R. Über die analytische Erfassung und Differenzierung von Acetaldehyd, Aldol und Glyoxylsäure, sowie deren Vorkommen im Diabetikerharn. [**The analytical determination and differentiation of acetaldehyde, aldol, and glyoxylic acid, and the occurrence of these substances in diabetic urine.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 129.

In severe diabetes very minute quantities of aldol may occur in the urine, but in the cases investigated it did not occur in significant quantity. The presence of acetaldehyde in diabetic urine was confirmed, but no glyoxylic acid was found. Dimethylhydroresorcinol (Dimedon) was used to detect the aldehydes.

H. W. D.

Kapfhammer, J. Über Bildung von Mercaptursäure im Eiweissminimum. [**The question of mercapturic acid formation in animals on protein-free diet.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 302.

When bromobenzene is fed to a dog simultaneously with protein it is excreted as p. bromophenylmercapturic acid. But if administered to a dog receiving no protein, none of this acid appears in the urine. If, however, cystein is injected simultaneously during the ingestion of the bromobenzene the mercapturic acid is excreted. Thus it appears that the cystein resulting from tissue breakdown is not available for the synthesis of mercapturic acid in the animal organism. In what form bromobenzene is excreted in the absence of the necessary cystein is not stated.

H. W. D.

Lusk, G. Animal calorimetry. 18. The behaviour of various intermediary metabolites upon the heat production. *J. Biol. Chem.*, 1921, **49**, 453.

Taistra, S. A. 19. The influence of acids upon the carbon dioxide combining power of the blood plasma. *J. Biol. Chem.*, 1921, **49**, 479.

The two papers deal with the question of the specific dynamic action of foodstuffs. It had been thought that the similarity of the rise of heat production upon giving alanine and lactic acid respectively, meant that the ingestion of these two substances had the same physiological effect upon metabolism. Further research, here recorded, has led to a change of this view. There appears to be no real relation between the height of the metabolism and the number of potential hydrogen ions administered. This negatives the view that the specific dynamic action is an effect of acid *per se*. The indications obtained from observations of the carbon dioxide combining capacity of the blood support the lack of correlation. Neutralized glycine produced a comparatively large rise of metabolism. The results leave the general problem of the meaning of amino-acid stimulation, if anything, more obscure. Some of the results obtained support the view that acetic acid is a normal intermediary product in the oxidation of fat in the body. R. A. P.

Heyer, G. R. Der Stickstoffhaushalt im Greisenalter. [**Nitrogen metabolism in old age.**] *Deutsches Arch. f. klin. Med.*, 1921, **138**, 76.

This paper is a contribution from the laboratory of Fr. Müller on the problem of senility, in which he has been interested for many years. An attempt was made to determine the nitrogen minimum in patients varying from 64–72 years of age.

The endogenous nitrogen excretion (nitrogen excretion on a nitrogen-free diet) was within the average limits which have been found by other observers in subjects of younger years. The minimum quantity of nitrogen required to bring the patients into nitrogen balance was about the same as is found in normal persons. The old people required a larger amount of nitrogen to obtain nitrogenous equilibrium than was lost on a nitrogen-free diet. While the endogenous metabolism of the aged subjects was in the higher limits, there was no evidence of a senile protein destruction.

C. G. L. W.

Ellinger, P. Beiträge zur Theorie der Kolloidreaktionen im Liquor cerebrospinalis. [**Contributions to the theory of the colloid reactions in cerebrospinal fluid.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 245.

Zsigmondy's original observation that proteins protect colloidal gold solutions from precipitation by means of sodium chloride forms the basis of tests applied clinically to the cerebrospinal fluid. Under certain conditions the fluid from cases of syphilis and meningitis reacts with colloidal gold solutions while normal fluid produces no change. The author uses 'collargol' instead of colloidal gold, and studies the best conditions for the reaction. The nature of the reaction is discussed and experiments are made to test various theories which have been put forward. H. W. D.

Meier, K. Über die aktuelle Reaktion des Liquor Cerebrospinalis. [**On the true reaction of the cerebrospinal fluid.**] *Biochem. Ztschr.*, 1921, **124**, 137.

In extension of the work of Parsons and Shearer upon the cerebrospinal fluid, it has been found that the reaction is slightly more alkaline than the blood, a P_H of 7·40. The CO_2 tension is the same or rather less than that in the blood. Cerebrospinal fluid contains less buffers than the blood. This means that it is less resistant to changes in the reaction induced by the addition of acid. Some pathological cases were investigated. In tabes dorsalis and a tuberculous inflammation of the meninges, there was no change in CO_2 capacity or reaction. A case of purulent meningitis showed a slightly lowered CO_2 tension and CO_2 capacity at a normal reaction. In a case of epidemic meningitis there was an actual acidosis in the cerebrospinal fluid (P_H 7·06). R. A. P.

Macht, D. I., and **Ting, G. C. Experimental inquiry into the sedative properties of some aromatic drugs and fumes.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 361.

The author has investigated some of those drugs which have for years been looked on by the medical profession and the laity as having sedative effects without much substantial pharmacological evidence. The method used was that of observing the behaviour of albino rats in a maze before and after treatment. Valerian and asafoetida produced a distinct sedative effect. The results from other substances, notably from various forms of incense, were doubtful. C. G. L. W.

Hesse, E. Über die Cyanamidwirkung. [**The action of cyanamid.**] *Ztschr. f. d. ges. exper. Med.*, 1921, **25**, 321.

In connexion with cyanamid, which has attained such great importance as an artificial fertilizer, it has been found that persons working with it are attacked by fleeting exanthemata of the head and chest. There is rapid breathing, increased heart action, and low blood-pressure. The attack lasts an hour or two. The curious feature of the attack is that it only comes on when the patient has consumed alcohol in some form.

It has been thought that alcohol increases the toxic effect of cyanamid, which is by itself considerable. This however is not the case.

Cyanamid is able to energize the action of a number of substances such as chloral hydrate, sodium bromide, theobromin, &c. For example: if a guinea-pig be given a small amount of sodium bromide which is physiologically inactive, followed by a small dose of cyanamid, there is an immediate action as if the animal had been poisoned by a large dose of bromide. In an experiment on a man a dose of cyanamid was taken in the morning, and in the evening, when the experiment had been quite forgotten, the subject took a glass of beer. The typical symptoms came on, the attack lasting six hours. The practical results are obvious, in that all persons working with this fertilizer should abstain from the use of all alcoholic drinks. C. G. L. W.

Macht, D. I., and **Ting, G. C. A study of antispasmodic drugs on the bronchus.** *J. Pharmacol. & Exper. Therap.*, 1921, **18**, 373.

Rings of pigs' bronchi were used in an attempt to correlate clinical experience with pharmacological findings. On the whole, the two methods

of observation are in agreement. The most powerful broncho-dilators are papaverine and various benzyl compounds, and secondly atropine, which exerts its action through paralysis of the para-sympathetic myoneural junctions, and thirdly epinephrin which produces active stimulation of the true sympathetic dilator terminals. The iodide, bromide, and nitrite produce a relaxation of the bronchial muscle. The action of various antispasmodic drugs on bronchial muscle varies in intensity with the previous tonicity or spasticity of the bronchus. A distinct difference has been found to exist between the behaviour of bronchi from healthy lungs and those showing pathological changes. C. G. L. W.

Winterstein, E., und **Iatrides, D.** Über das aus Taxus baccata, Eibe, darstellbare Alkaloid, Taxin. [**Taxine, the alkaloid of the yew (*Taxus baccata*).**] *Ztschr. f. physiol. Chem.*, 1921, **117**, 240.

The toxic alkaloid of the yew, taxine, occurs in the greatest quantities in the needles. The formula $C_{37}H_{51}O_{10}N$ is given to the substance, but it is doubtful whether the preparation is pure, since no crystalline product was isolated. Cinnamic, acetic, benzoic, and oxalic acids, benzamide and benzonitrile were isolated from the products of hydrolysis and oxidation.

The alkaloid is a specific poison for the heart. Death occurs with convulsions and a fall of blood-pressure. The lethal (intravenous) dose for rabbits is 0·004–0·005 gm. per kilo body-weight. It causes a quickening of the pulse, respiration and intestinal movements, and a slowing of the heart's action. H. W. D.

Cannon, W. B., Rappert, D., and **Uridil, J. E. Studies on the conditions of activity in endocrine glands. VI. Further observations on the denervated heart in relation to adrenal secretion. VII. The reflex centre for adrenal secretion and its response to excitatory and inhibitory influences. VIII. Some effects on the denervated heart of stimulating the nerves of the liver.** *Am. J. Physiol.*, 1921, **58**, 308, 338, 353.

The adrenal medulla is subject to reflex stimulation. The reflex centre is situated immediately posterior to the corpora quadrigemina in the floor of the fourth ventricle. This is in agreement with the results obtained by Elliott and by Anrep. This centre is subject to inhibitory influences which reach it by the vagus or the depressor nerves. In the third paper the interesting observation is made that stimulation of the hepatic nerves liberates a substance from the liver which causes the heart to beat faster even when the adrenals are absent. This effect is more distinct in well-fed animals than in fasting animals. A further communication on this point is promised.

These three papers also contain much controversial matter, since they represent a continuation of the controversy which has been going on for a considerable time between Cannon on the one side and Stewart and Rogoff on the other. The latter authors deny that the adrenal glands secrete adrenalin as the result of reflex stimulation and admit only a slight continuous secretion of adrenalin. Cannon refutes in these papers the criticism which Stewart and Rogoff have raised against his method of inferring an increased secretion of adrenalin from an increased rate of the denervated heart.

(Note of abstractor.—The point in dispute has been conclusively settled

by the histochemical demonstration of a secretion of adrenalin by reflex stimulation under natural conditions, i. e. in an intact animal without the use of an anaesthetic and using stimuli which normally affect the organism —cold, fever, &c.). W. C.

Lindenberg, Ad., and **Pestana, B. R. Chemotherapeutic studies with fats of acid-fast bacilli.** *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, **32**, 66. (*Chem. Abstr.*, 1921, **15**, 3327.)

Chaulmoogra oil and many other oils, because of their content of unsaturated fatty acids, have an inhibitory action upon cultures of tubercle bacilli and other acid-fast organisms. This probably accounts for the therapeutic efficiency of chaulmoogra oil in leprosy and cod-liver oil in some cases of tuberculosis. These oils act as direct chemotherapeutic agents and not as stimulators of phagocytosis. The chaulmoogra oils obtained from *Taraktogenus kurzii* are not only most efficient therapeutically in the treatment of leprosy, but possess the greatest inhibitory power against cultures of acid-fast organisms. The activity of the oil is due to the unsaturated acids, but not all these acids possess the same degree of activity. Cultures of lepra and tubercle bacilli also contain unsaturated fatty acids. It is therefore wrong to attribute the activity of the fatty acids to the action of the unsaturated fatty acids alone. It is possible that the activity is proportional to the number of double bonds in the acid molecule, or it must be assumed that the active oils contain an unknown, unsaturated fatty acid, or an homologous unsaturated fatty acid, not yet isolated. C. G. L. W.

Felix, K. Über Eiweissderivate basischer Natur. [**Protein derivatives of basic character.**] *Ztschr. f. physiol. Chem.*, 1921, **116**, 150.

From intestinal mucosa, lymph, and thymus glands, protein derivatives have been prepared which are resistant to the action of trypsin. They are strongly alkaline to litmus and have a high content of hexone bases. They are not precipitated by ammonia, potassium ferrocyanide, Witte peptone, or nucleic acid, as are the histones, and they display a red-violet biuret reaction. H. W. D.

Gilbert, O. Über die Darstellung von Phosphorsulfatiden aus Gehirn. [**On the preparation of phospho-sulphatides from the brain.**] *Biochem. Ztschr.*, 1921, **124**, 206.

Sammartino, U. Über die Chemie der Lunge. [**On the chemistry of the lung.**] *Biochem. Ztschr.*, 1921, **124**, 234.

Thudichum and others since have described the presence of a sulphur-containing substance in the white precipitate from an alcoholic extract of the brain. This has not so far been given a constitution. In this paper the author describes the preparation of a barium salt of a phosphosulphatide (isolated from the human brain). He gives to it a constitution of $C_{93}H_{187}N_3SPBa_2O_{18}$.

In a paper by Sammartino upon the chemistry of the lung, besides the demonstration of the presence of lecithin and cephalin, it is claimed that

there is present a comparatively large amount of cerebroside and of phospho-sulphatides. It would therefore appear that these bodies are of some general significance, and it will be interesting to know what is their exact biochemical function. R. A. P.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

Owen, E. A., and **Bowes, P. K. X-ray dosage, with special reference to the barium platinocyanide pastille.** *J. Röntg. Soc.*, 1921, **17**, 107.

This paper is the first of a series in which the various methods of measuring the intensity of a beam of X-rays, i. e. ionization, production of heat, fluorescence, chemical and electrical changes, are to be correlated. In each case a comparison is made with the ionization method as being the most accurate. The present paper deals with the barium platinocyanide pastille.

The ionization produced by a narrow beam of X-rays from a Coolidge tube enclosed in a leaden box, was measured by the rate of fall of the gold leaf of an electroscope. The electroscope was standardized by noting the effect produced by the γ-radiation of a known quantity of radium bromide at a fixed distance. At the same time a pastille was exposed to the radiation from the X-ray tube and the change of tint produced in a certain time compared by means of a Corbett tintometer. For this observation the time for a standard β-dose could be calculated. In one series of experiments the voltage and frequency were kept constant and the current varied, in a second series the voltage was varied and the current kept the same. In both cases the two methods of measurement gave exactly the same information as to the output of energy in the form of X-rays, under different conditions of current and voltage. For the voltages employed (up to 90 kilowatts) the intensity, and hence the time of dose, was found to be approximately proportional to the square of the voltage applied. The action of different types of interrupter (the Sanax, mercury jet, and dipper types) was next investigated, also variation of the frequency of interruptions, and in both cases the pastille agreed with the ionization method. In conclusion, a short outline is given of a method of standardizing the barium platinocyanide pastille. B. D. W.

Gough, H. B. Methods of measurement of high voltage. *J. Röntg. Soc.*, 1921, **17**, 126.

The practice of estimating voltage by means of the voltage necessary to break down a needle-point spark-gap has been shown to be unreliable, as the readings are affected by variations in pressure, temperature, sharpness of points, &c. Quadrant electrometers are useless above 14,000 volts, owing to sparking taking place. Two forms of electrostatic voltmeter are described,

constructed by Abraham and Siemens and Halske, working on the principle of the attraction between two insulated plates, as in Lord Kelvin's volt balance. These instruments are large and costly. The sphere-gap voltmeter devised by Kaye does not suffer from these defects, and has only the slight drawback that it must be operated by hand whilst the instrument is working.

With transformer sets the secondary voltage across the X-ray tube can be measured by an auxiliary winding of a few turns on the yoke of the transformer itself, the E. M. F. induced in this winding being measured by an ordinary voltmeter. The readings of the instrument are found to vary with the current as much as 10 per cent. in certain cases. A voltmeter was calibrated by means of a sphere-gap voltmeter, and the scale modified so as to give the true voltage at various current strengths. B. D. W.

Tyndall, A. M., and **Hill, E. G. A new form of stereo-fluoroscope.** *J. Röntg. Soc.*, 1921, **17**, 122.

This instrument is designed to produce a stereoscopic effect in the picture viewed on the fluorescent screen. The X-ray tube is mounted in a special carriage which moves rapidly backward and forward in a horizontal line, being driven by simple mechanical gearing. In front of the face of the observer, a disk with a sector of 90° removed is revolved in time with the vibrations of the tube. It is so arranged that one eye is uncovered at the end of the travel of the tube, and sees the picture produced by the anti-cathode in that position. The other eye is then uncovered by the revolution of the disk and sees the picture produced at the other end of the movement of the tube. The rapid alternation of the two pictures produces the effect of a continuous stereoscopic picture. This apparatus has the advantage that an ordinary form of tube is employed in contrast to the tubes with a double anticathode alternately excited, which have been designed to give the same effect. B. D. W.

Radiodiagnosis

Lorenz, H. Zur exacten Diagnose des Ulcus duodeni. [**The exact diagnosis of duodenal ulcer.**] *Fortsch. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 1.

At a meeting of the Society for Diseases of the Digestive and Metabolic Systems, held in Homburg in 1920, a combined discussion was held by physicians, surgeons, and radiologists upon duodenal ulcer By the clinicians radiological diagnosis was held to be of little value and many of the more recent methods of radiological diagnosis did not come under review. Lorenz has taken up the subject anew and asserts that in the Röntgen Institute of the University of Hamburg, under the late Professor Albers-Schönberg, alterations in the wall of the 'bulbus' indicated duodenal ulcer in approximately 70 per cent. of cases, of which 66 per cent., i. e. 33 cases out of 50 in which duodenal ulcer was determined by operation, had previously been diagnosed as such radiologically. The details of the observations must be read in the original paper, but the following table gives a general survey of the percentage frequency of various signs noted in different varieties of case.

	Ulc. Duod.	Ulc. Pyl.	Ulc. Praepyl.	Ulc. Call. S. Pen. Part. Pyl. Vent.	Ulc. Call. S. Pen. Curv. Min.
Number of cases	50	9	7	7	21
	%	%	%	%	%
Hyperistalsis	74	55	43	71	33
Hypersecretion	42	44	60	14	33
Hypertonus	ca. 70	22	14	—	—
Deficient mobility	56	44	71	71	72
(*a*) traces only	47	33	28	—	48
(*b*) some	13	11	43	—	23
Ectasis	26	22	30	43	33
Ptosis without ectasis	30	44	14	29	29
Traction to right	24	33	14	—	5
Early pylorospasm	20	44	14	14	14
,, ,, insufficiency	10	11	—	14	24
Bulbar defect	53	44	30	—	—
Distortion of pylorus or antrum	14	55	71	—	—

W. S. L.-B.

Guénaux et Vasselle. Technique de l'examen radioscopique du duodénum. [**The technique for radioscopic examination of the duodenum.**] *J. de radiol. et d'électrol.*, 1921, **5**, 443.

The authors point out the difficulty of examining the duodenum because of its being hidden behind the stomach, deeply situated, on four different planes, and lastly because the opaque substance enters in small quantities at a time. They believe their technique overcomes this. They examine the duodenum with the patient placed in various positions, frontal and oblique, standing up and lying down: of these, the right anterior oblique in the upright position and the left posterior oblique lying down are the most favourable.

Preparation of the patient. The patient's normal habits are not interfered with previous to the examination, but all drugs which might influence the motility of the alimentary canal or be a cause of error, e.g. bismuth, are omitted. A purgative is not needed unless there is marked constipation. The authors disagree with Kreuzfuchs that no food should be taken during the previous twelve hours, and frequently employ the method of the double meal, and prefer it to the method of multiple meals, which often leads to error in duodenal cases as the transverse colon may mark the duodenum.

Choice of the opaque substance. This is considered important and the authors use creamy barium sulphate which is chemically pure barium sulphate obtained by a special process: the salt does not form a sediment, and the shadow is very clear.

Examination of the patient. The morning is the best time. A patient who is to be examined in the middle of the morning takes the opaque meal about 4 a.m. and remains fasting till the examination. Before the examination is made the whole abdomen is examined. (1) **Upright position.** (a) *Anterior frontal position.* Having made certain that all the first meal has left the stomach and noted which portion of the intestine it has reached, the patient is given a second meal and the stomach is examined, particular note being taking of the peristalsis and mode of emptying. Mention is made of what the authors call the 'pyloric surprise'; it is some minutes after this has occurred that the true emptying of the stomach begins and continues regularly. By this examination the topography of the duodenum

can be determined and a preliminary study made of the passage of the meal. The various portions of the organ can only be examined very incompletely ; a description of what is seen in various types of cases is given, and the authors state that to dissociate the various shadows of the stomach and duodenum the right anterior oblique position is necessary. (b) *Right anterior oblique position.* The patient is turned through about 45° so that the right shoulder is against the screen and the duodenum appears in a clear space between the vertebral column behind and the stomach in front. This brings the whole duodenum into view, but particularly the duodenal bulb, the sub-hepatic angle, and the fourth part. It is the only position in which the sub-hepatic angle can be seen. (c) *Other positions.* In most cases examination in the above two positions is sufficient. In some cases the left anterior oblique position may help to distinguish the shadows of the stomach and duodenum. The posterior frontal position shows enlarged images which is of use when studying deformities of the organ. (2) **Lying down.** (a) *Lying on the back.* This gives variable results: painful points can be localized more easily than when the patient is standing up. (b) *Lying on the abdomen.* The position of the patient is described. In this position the abdominal organs are more displaced than when the patient is lying on his back. The appearance of the stomach is described. The passage of food into the duodenum can be clearly seen and the examination is made easier by the enlarged images. Often, however, the pyloric region is compressed by the vertebral column, and for this reason the authors prefer to combine two positions as follows: (c) *Left posterior oblique position while lying on the stomach.* In this position the various portions of the duodenum are more completely filled and the physiological action of the organ is clearly seen. The position can be maintained for a long time without fatigue, and is one in which it is easy to percuss the seventh cervical vertebra, which, according to Lebon, aids the emptying of the stomach. The only disadvantage of the ventral position is that the painful points cannot be examined ; a method for overcoming this is described. (d) *Lying on the side.* This is of no use. The left posterior and oblique position while lying on the stomach affords the same advantages as lying on the right side and avoids the disadvantages.

Manipulations for artificially bringing about the filling of the duodenum. Pressure on the lower part of the greater curvature of the stomach is of use when the stomach empties slowly. Mention is also made of Case's manipulation, but the authors state that in the majority of cases an examination in the left posterior oblique position while lying on the stomach renders this of no use. P. L.-B.

Vogt, E. Die Röntgendiagnostik der Bronchopneumonie der ersten Lebenszeit. [**Röntgen diagnosis of bronchopneumonia in newly-born infants.**] *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1921, **28**, 54.

Clinical diagnosis of broncho-pneumonia in newly-born infants is difficult, says Vogt, a fact which is well known to the medical fraternity. Fever, heavy breathing, dilatation of the nostrils in breathing, cyanosis, and attacks of choking must, however, always point to pneumonia. Cough is generally absent. Oddly enough, Röntgen diagnosis of this disease in the newly-born is but little known, even among child specialists, although it is as easily revealed in babies as in adults. The writer's first case was made public in 1914, and in the present communication he gives two other instances, the one determined by autopsy, the other in process of healing.

The technique for the diagnostic process in lung affections differs. The best results are achieved with instantaneous photography on the Dessauer system, the time of exposure being only one two-hundredth of a second. The usual time of exposure under rays is one-tenth second, but this does not give such clearly defined results owing to movement of the diaphragm and vibration of the thorax through heart contraction and pulsation of the large tubes.

This success of Röntgen diagnosis in infantile lung affections, the writer says in conclusion, should prove of infinite value as thereby in many cases it may be the means of saving some and is of real practical value from a clinical point of view. F. E. R.

Radiotherapy

Fischer, J. F. The Roentgen treatment of morbus basedowii. *Acta Radiol.*, **1921, 1, 179.**

In the beginning of his paper the author refers to the literature upon the subject of his paper, giving references. In all, the author has treated 490 cases: 231 of these were private cases, of which a third were somewhat doubtful, a third slight, and a third severe cases of the disease. A case to illustrate the difficulty in diagnosis is given and discussed. Out of all the cases only 11 were men, the majority of the patients were between 30 and 45 years, and the duration of the disease for the most part from 6 months to 5 years. In discussing the cases the author states that those treated at hospital and those treated privately must be kept apart as they are in different social positions, which is of importance. Those treated in hospital usually are persons who earn their living by physical labour, and this increases the risk of contracting the disease. The method of treating private patients is given. Recurrence nearly always occurs in hospital cases, and the author states that this is due to overwork or domestic troubles. Taking the patients as a whole, four-fifths have benefited from the treatment and the remainder, even if no better, have not changed for the worse: only one case died. Patients in whom tachycardia predominates over the nervous symptoms are those in whom X-ray treatment is most likely to fail.

Fourteen cases are then described with moderately full notes and in each case at least two photographs are given, one before and one after treatment.

According to the author, improvement begins after the first series of irradiations: weight should be observed, and in almost all cases where the patient is deriving benefit there is an increase in weight, often occurring about a month after the beginning of the treatment; at first there may be a small loss of weight. The effect of treatment on the various symptoms and the duration of benefit is related.

Complications of X-ray treatment are next dealt with, particularly whether there is any danger to the patient: the author believes that there is none if treatment be carried out by skilled hands. The cases which die are those in which the disease is severe, and in them spontaneous hyperthyroidism may occur with no treatment, as is shown by a case quoted. It is not denied that in some circumstances X-rays may have an unfavourable effect. As regards dosage, the author agrees with the vast majority that small doses are advisible in severe cases so as to avoid X-ray sickness; he

quotes Nordentoft, who says that small doses would tend to cause hyperthyroidism, whereas large doses would not. The fact that the patient's skin is always very sensitive demands caution as a smaller dose than might be expected will often cause erythema. Various other possible complications are mentioned. The technique is then described.

After discussing at some length the views of various authors on the question of surgical and X-ray treatment in these cases, the author gives his own views on the X-ray side of the question and considers it far preferable, and says it should always be used unless there is a danger in putting off an operation, which he considers to be a very rare event.

P. L.-B.

Gunsett, A. Considérations sur les doses en radiothérapie profonde ; méthodes françaises—méthodes allemandes. [B.] [**Considerations regarding doses in deep radiotherapy : French and German methods.** *J. de radiol. et d'électrol.*, 1921, **5**, 543.

The author reviews the three great stages in the evolution of radiotherapy. He states that the best rays for deep therapy are those of very short wave-length, corresponding to 0·2 Angström units, and that very heavy screening is necessary to cut out all the softer rays. To produce these rays 200,000 volts or more are needed. The French and German apparatus is shortly compared.

The dose in cancer. Uterine cancer above all other types has benefited from treatment with the new apparatus; the reasons for the usefulness are pointed out. It is mentioned that Nogier states that during prolonged treatment the tumour becomes immune to the rays, and that therefore the greatest possible influence should be brought to bear on the tumour at once. Acting on these lines the author has treated extensive and deep cutaneous epitheliomata with 20 H units or even 30 H units, using 4 mm. aluminium screen with very satisfactory results. As regards deep carcinomata, 15 H units filtered by 4–5 mm. of aluminium seems to be the limit which the skin can stand, but unfortunately this is not sufficient to kill the tumour, as the author estimates that only about 10 per cent. of the dose at the skin reaches the tumour. The séances have to be repeated with the consequent possible dangers. The doses employed by various authors are discussed at some length : working on the method of Seitz and Wintz, the author states that his results were deplorable, and that many German authors agree with him. It is pointed out that in treatment the dose is only one factor to be considered. After further discussion of the German methods it is stated that in France deep therapy with 10–12 mm. aluminium filters is being used more and more, and that 30 H units is generally considered the largest dose able to be used without damage to the skin.

The dose in non-cancer cases. The author says that in these cases the Germans are very mistaken in trying to apply the same methods as those applied in cases of cancer, and that in doing so they have done more harm than good. Non-malignant cases, if susceptible to radiotherapy, are more so than malignant cases with the exception of certain carcinomata; their method of reaction is explained, from which it follows that only relatively small doses are necessary. From this the author states that the new methods will not be of any great benefit, and compares the French and German results in cases of leukaemia. He has given up the German method entirely and

gives small doses once a week, which is the usual French method, and he states that the results are far better. To illustrate this he reports on 230 cases of tuberculous adenitis treated by the German method, and 200 similar cases treated by the French method of 3 or 2 H units applied every week. The same applies for tuberculous peritonitis and bacillary arthritis and osteitis. *Diseases of ductless glands.* Here too the author has reverted from the method of large doses infrequently to small doses at frequent intervals. In cases of goitre 8–10 séances are usually sufficient and the method applies equally well in hypertrophy of the prostate. *Diseases of the blood.* Here too small doses are used, particularly in leukaemia, in which disease a dose of 3 H units filtered by 4 mm. of aluminium is the largest that is applied to a single field each day and the blood reaction is closely watched. *Uterine fibroids and haemorrhage.* The German methods are discussed; all are heavy doses. Following Béclère, the author now uses doses of 3 H units with excellent results. In other diseases too, mediastinal tumours, neuralgias, &c., the author has reduced the dose with good results.

P. L.-B.

Brock, W. Welche Bedingungen sind massgebend für die Röntgenbehandlungen der Hautkrebse? [**Which factors are decisive in the Roentgen treatment of skin-cancer?**] *Strahlentherapie*, 1921, **13**, 1–40.

This article gives details of the treatment of 40 cases, and discusses the factors of site, histology of the tumour, radiation dose and interval, and the reactions of the tissue-bed and the related lymph and endocrine glands. (1) Frontal and parietal cancroids: Cases 2 and 4 were healed in the one instance by two doses of 40 X (Kienböck), 4 mm. Al filter, and in the other by one dose of 60 X (110 per cent. HED) (skin erythema dose). Both were squamous in type. In Case 1, a rodent, insufficient dosage was given at first, and further prolonged radiations caused an X-ray ulcer. Case 3 was, owing to the curvature of the forehead, wrongly treated at first (one field, too close focus-skin distance), the centre healing and the periphery spreading: this was later cured by a two-field radiation with 0·5 mm. zinc and 2 mm. Al, each 40 X. (2) Eyelid cancroids: 17 of these were treated, 14 of them having had unsuccessful operations. 16 were healed with one or more doses of 40 X, 4 mm. filter, which in a few cases were combined with stimulation doses to the thyroid, thymus, and ovaries (5 X, 1 mm. Al; 6 X, 3 mm, Al; and 8 X, 4 mm. Al respectively). One case was given too many small and large doses, with a Röntgen-ulcer following, which was cured by operation. In all cases with enlarged pre-auricular or sub-malar glands these subsided *without* radiation as the irradiated primary resolved. The technique of lid-cases given includes corneal protection with a prothesis and protection of the surrounding skin with bismuth-paste. (3) 15 nasal-cancroids, all of which did well with a similar radiation, one being a lupus-carcinoma. In several of these cases radium or mesothorium was alternated with the X-radiation, but the author prefers X-rays owing to the difficulties found in administering with radium capsules a sufficient dose to the periphery of the area treated, without burning the surrounding skin (the maximal radiation from a capsule being central). (4) Cancroids in the neighbourhood of the ear: 4 of the 5 cases died of cachexia or general metastasis, and the author considers the site the most unfavourable (unless over the mastoid) because the unavoidable radiation of the parotid, neck, and tongue glands causes

more general harm than local good, the liability to general metastasis being greatly increased by the radiation, in his view. Such cases therefore should be treated entirely surgically, in contradistinction to those in other sites. (5) 6 cases of cancroid of the lip (5 of whom had been repeatedly operated on or injected): with one exception (an extensive old-standing case of papillomatous epithelioma with large gland involvement before radiation treatment began, which also wrongly had a gland-stimulation dose before the primary had been sufficiently influenced), these cases were clinically cured with maximal dosage, cross-fire technique, and half-doses to the glands when these were slightly enlarged, e.g. 50 X from without, 30–40 X from the inner aspect (the tongue and glands shielded with guttapercha-covered lead plates), and 20 X to the glands in the floor of the mouth, a 4–5 mm. Al filter being used, and the dose repeated in a month or longer. (Bad results had been previously found in lip cases, but then the glands had full doses.) (6) Cancroids of the cheek: 6 cases all clinically cured with doses of 110 per cent. skin dose.

The author concludes that if the tumour is in a region poor in glands, i.e. in a tissue-bed of low radio-sensibility, the prognosis is excellent if a proper technique be employed, maximal highly-filtered doses in one sitting, repeated in 2 or 3 months, giving the best result (with heavy doses and 1 mm. Al filter, recurrence had been seen in 6 weeks). This 110 per cent. skin-dose, however, is only *one* factor in the result, as the unsuccessful cases in front of and below the ear show; for the filtering effect of the related glands is necessary for a cure, and probably also the endocrine glands' integrity. The distinction must be drawn between obvious gland-metastases and probably carcinoma-free glands. The former are as hopeless radiologically as surgically, as gland-cells are more radio-sensitive than epithelial cells, and enough of a radiation to damage the latter will seriously damage the gland, and with it its protective faculty against general metastasis, which in the author's ear cases rapidly made its appearance: gland-metastases therefore are better left alone radiologically, at least unless or until the primary has been destroyed. But probably uninfected or slightly infected glands should have a stimulation dose, by which the likelihood of cure will be increased. The experiments and views of Kaminer, Theilhaber, and others are discussed, which suggest the importance of the round cells, thymus, spleen, ovaries, &c., in the general resistance to malignant invasion, and the author concludes with a plea for the more detailed study of the general biological factors in tumour-radiation, saying that too much relative importance has been paid so far to the physical factors, while the biological factors considered have been too much restricted to the skin-reactions and the effect on the tumour *per se*. J. H. D. W.

Nordentoft, S. Tilfælde af Mb. Basedowii. [**Cases of Graves's disease.**] *Hosp.-tid.*, 1921, **64**, 31.

Nordentoft's advocacy of the Röntgen treatment of Graves's disease is whole-hearted; of 150 cases thus treated, the first dating back 5 years, he has not lost one, not one has become worse, and hardly any have remained stationary. Nearly all were cured or on the way to being so. Referring to 3 Röntgen fatalities associated with Graves's disease and published in the Danish medical press, he expressed doubts as to death being due to, or even hastened by, the X-rays. With regard to technique, he prefers large

exposures at long intervals to frequent small exposures. On no pretext should the thymus be excluded from the area under treatment. C. L.

Trier, K. Tilfælde af Mb. Basedowii. [**Cases of Graves's disease.**] *Hosp.-tid.*, 1921, **64**, 48.

Between 1913 and 1920 Trier has treated about 200 cases of Graves's disease at the Röntgen department of the Rigshospital in Copenhagen. In the course of two months he has personally examined 88 of these patients, and he has received reports on several others. A comparison of the results showed that there was little to choose between giving: (1) small exposures over a considerable period; (2) small exposures over a considerable period, the thymus being included, and (3) big exposures, both the thyroid and thymus areas being included. Trier's opinion of the value of X-ray treatment is guarded; it may be an excellent supplement to general medical treatment, giving this in many cases just the support needed to tip the scales in the patient's favour. But it is not of epoch-making importance, and it seems to matter little whether the thymus is treated or not. C. L.

Electrotherapy

Bordier, H. New conceptions on the treatment of infantile paralysis. *Arch. Radiol. & Electroth.*, 1921, **26**, 215.

The author, in agreement with others quoted, does not believe that the disease need necessarily lead to complete crippledom if properly treated. He reviews the appearance of the cord in the portions affected. In his view the logical therapeutic indication is to act on the medullary lesion by radiotherapy, as he asserts that it must have the effect of re-establishing the cells incompletely destroyed, and of arresting the progress of the poliomyelitis. Treatment must be undertaken as early as possible. The author employs a series of three consecutive radiations once a month with 5 mm. Al screen. The second point is to combat the lowering of the temperature of the affected limb, and for this purpose diathermy is the most efficacious means: various other methods tried are enumerated. The technique is described. Treatment is continued for four or five days, after which the limb retains the warmth; this is the time to begin electrical treatment. If necessary, diathermy is repeated. The electrical treatment may have to be continued for months or years. P. L.-B.

Cluzet et **Bonnamour.** Étude électrocardiographique de l'arrêt du cœur dans l'électrocution. [**Electrocardiographic studies of the stoppage of the heart in electrocution.**] *J. de radiol. et d'électrol.*, 1921, **5**, 529.

The paper is the result of experiments carried out on dogs and rabbits electrocuted by a constant current of 110 volts and 0·5 ampère, in which, when the heart showed tremors or had stopped beating, massage and intravenous injections of 5 per cent. potassium chloride were used to try and restore the heart-beat. The current was passed from mouth to rectum. A description is given of the effects of passing the current for about one second and one to two minutes: tracings in the latter case are differentiated from those obtained in auricular fibrillation. In some cases, after both auricles and

ventricles were absolutely motionless, the tracing showed large oscillations; this electric activity may persist 5 to 10 minutes after muscular activity has ceased. As regards restoring the heart-beat, the authors have succeeded in restoring auricular contraction with ventricular tremor in one case, but fail to find the method of such 'marvellous efficacy' as Halluin described it. They state that the tracings of the heart-tremor as a whole or those of the auricular tremor are quite distinctive, and describe them. Thirteen tracings are included. P. L.-B.

Bergonié, J. Action de l'ergothérapie passive sur la circulation. [**The action of passive ergotherapy on the circulation.**] *Arch. d'électric. méd.*, 1921, **29**, 257.

The author begins by describing what is meant by passive ergotherapy. He states that the immediate effect of every muscular contraction is the release of energy in the form of mechanical work or of heat, and of all the processes by which the energy is prepared or brought to the muscle, the circulation is most directly dependent upon muscular contraction. A short review of the research done to show that increased blood-supply always accompanies increased work follows. After comparing voluntary muscular contraction with passive ergotherapy, he states: (1) that muscular contraction produced electrically is identical in its results with voluntary contraction except in so far as the nervous system is concerned; (2) that it can be just as powerful; (3) that, more generalized and regular, it is able to produce circulatory and metabolic modifications at least as intense as the most violent exercise, and that for a longer period. If anything, the author considers that a muscular contraction produced electrically is more efficacious in aiding the return of the blood to the heart than one produced voluntarily, since it is more generalized. According to him it is a 'peripheral heart'. In conclusion, it is stated that passive ergotherapy can be used by, and is directly under the control of, the physician as the best method of modifying the activity of the circulation. P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEW

SYPHILIS

Symptomatology. Oltramare, of Geneva, has observed 19 cases of *reinfection with syphilis,* one of them a case of double reinfection, during the last five years. He thinks that reinfections have become more frequent since the introduction of treatment with arsenobenzol compounds, and that probably more cases are cured. Belgodère, however, reports a case of reinfection in a patient who had a chancre and secondary syphilis fifteen years previously, and was treated with mercurial injections only. The conditions necessary for a diagnosis of reinfection, according to Oltramare, are (1) the occurrence of a chancre containing *S. pallida* after the usual incubation period and with characteristic adenopathy in a patient known to have had syphilis; (2) a negative serum reaction which becomes positive before the appearance of secondary symptoms. In one of his cases this did not occur till $2\frac{1}{2}$ months after the chancre. It is unnecessary and unjustifiable to wait for secondary symptoms before commencing treatment. He points out that the situation of the new chancre in the scar of the first chancre does not necessarily signify a redux chancre and rule out reinfection. In one of his cases this occurred, but another chancre developed simultaneously in another place.

Oltramare gives details of 19 cases which conform with the above conditions; other cases were probable but incomplete. In all but two both infections were observed personally. If reinfection is to be regarded as a proof of cure, one would expect some guidance from the previous treatment of cases which become reinfected. Oltramare's cases, however, furnish no such guidance. In the first place, 8 of his reinfections occurred in patients who had commenced treatment during the primary negative, and 7 during the primary positive stage. It would appear, therefore, as easy to cure syphilis in the one stage as the other. Secondly, the previous treatment of his cases varied in the extreme. In one case a single injection of 0·90 gm. neosalvarsan was the only treatment given; in the other cases the number of arsenical injections varied from 2 to 17, and the totals of the drug administered from 0·90 to 10·20 gm.; in 7 cases neosalvarsan was the only drug given, and in 12 mercurial treatment, usually by injections of the salicylate, was given in addition. The dates of reinfection varied from three months to six years after the original infection, being less than a year in 9 cases.

The details of the case of double reinfection are as follows: October 1917: mixed chancres of coronal sulcus, spirochaetes absent owing to cauterization, Wassermann reaction positive, adenopathy characteristic; after 8 injections of novarsenobenzol and 12 of mercury salicylate, Wassermann reaction negative. May 1918: chancre of coronal sulcus, spirochaetes present,

Wassermann reaction negative; 10 injections of novarsenobenzol. September 1920: chancre of prepuce, spirochaetes present. Incubation of chancre 30 days, confrontation with woman positive for syphilis. Wassermann reaction at first negative, both in blood and cerebrospinal fluid, afterwards positive, finally negative after treatment with neosalvarsan and mercury salicylate. Intervals between first and second infections seven months, between second and third two years and five months. First two infections observed by Oltramare, third by Bloch, of Zurich. The second reinfection differed in no way from the first as regards incubation, evolution, and reaction to treatment. Oltramare points out the importance of distinguishing redux chancre from reinfection, especially as the former has become more common since salvarsan was introduced. Spirochaetes may be present and the Wassermann reaction may be negative in either case, but the characteristic adenopathy is absent in redux chancre, and this seldom develops after two or three months. On the other hand, he does not think a short interval or inadequate treatment sufficient to rule out a case of reinfection. He thinks it is going too far to look upon reinfection as a proof of sterilization of the organism, and remarks upon the difficulty in distinguishing between superinfection and reinfection.

Finger discusses the question of the differential diagnosis between cases of true reinfection and cases of redux chancre and the pseudo-chancre of Fournier. As the former occurs in the scar of the original chancre a few weeks after healing, diagnosis is easier than in the case of pseudo-chancre, which may not appear for several years. According to Finger, however, a second chancre appearing after a short interval in the scar of the first is not necessarily a redux chancre, for the scar is more easily eroded and open to reinfection. A long interval, during which the patient has been free from clinical or serological signs of syphilis, favours the probability of true reinfection; but it is only a probability and cannot be proved. Laboratory diagnosis does not decide the question, for although the presence of numerous spirochaetes in the second chancre suggests a new infection and a sparcity of spirochaetes, a redux chancre or pseudo-chancre, spirochaetes are not always easy to find in a true chancre. Neither is the Wassermann reaction decisive, for it may be at first negative, changing later to positive, in both instances. According to Finger, the only cases which can be regarded as true reinfections are those which occur in cases of primary negative syphilis which have undergone an abortive cure and remained negative all through treatment. Logically, the second infection should be followed by typical regional adenitis and a roseola. In cases of primary positive syphilis and those with secondary symptoms, however, Finger is of opinion that a true reinfection cannot be definitely accepted even if the second chancre is followed by regional adenitis and secondary symptoms; for, under the influence of time and treatment, the immunity conditions are so altered that the organism can react with local recrudescence of the original spirochaetes followed by generalization, in the same way as it does to infection from new spirochaetes, and we have no means of distinguishing between the two conditions. It is true that localization of the two chancres in different parts of the body, the first on the genitals and the second on the lips, for instance, would be in favour of reinfection, since the majority of pseudo-chancres occur on the genitals; but it is not conclusive, for, according to Fournier, and also Finger, pseudo-chancres may occur on the lips, tongue, and other parts of the body. According to Finger, therefore, in the majority of cases

it is impossible to decide whether a given case is one of true reinfection with external spirochaetes or one of recrudescence of the spirochaetes of the original infection. All we can do is to weigh the probabilities, taking into account the general course of the two infections, the interval between them, the relative situations of the two chancres, and the intensity of treatment of the first infection. Finally, the experiments which Finger conducted with Landsteiner tend to show that constitutional syphilis, while still uncured, is not completely immune to fresh infection with new virus from without.

Gougerot discusses the question of *acquired syphilis without chancre*, and gives details of two cases in which no evidence of a primary chancre was found. In the first case the first lesion observed was a suppurating bubo resembling chancroidal bubo. Examination for Ducrey's bacillus, however, was negative, both microscopically and by culture. Auto-inoculation was also negative. A few *S. pallidae* were found in serum from the glands. The Wassermann reaction became positive 30 days after the appearance of the bubo, and secondary syphilis followed. The bubo appeared 29 days after coitus with a woman infected with secondary syphilis, no chancre being discovered. In the second case the first sign was a typical indurated inguinal adenitis. No chancre was found on the genitals or anus. The adenitis appeared one month after coitus with a woman suspected of syphilis. *S. pallida* was found by gland puncture, and secondary syphilis developed two months later. Gougerot concludes that syphilis may begin without a chancre, either as an indurated or a suppurating bubo, and advises that all such cases should be examined for *S. pallida* by gland puncture and by repeated Wassermann tests.

Warthin and Noland report six cases of chancre and eight of later syphilitic lesions of the *cervix uteri*, which were diagnosed as carcinoma. In one of these hysterectomy was performed, after which secondary syphilis appeared, and the patient brought an action for damages for infection in hospital. The details of this case, which is interesting both from the medico-legal and pathological points of view is as follows: patient aged 42; cervix covered with a cauliflower ulceration, bleeding easily, and covered with a grey membrane; uterus retroverted, adherent, and rather enlarged; Wassermann reaction negative. Diagnosis probable carcinoma. Two months later secondary syphilis appeared with a positive Wassermann reaction. Microscopical examination of the cervix showed no evidence of malignant growth. In the outer zone there was plasma-cell infiltration formed by proliferation of endothelial cells, especially of the lymphatics and terminal capillaries. In the deeper zones there was proliferation of lymphatics, perivascular infiltration, and thickening of the arterioles. *S. pallida* was found by Warthin's silver nitrate stain (*Medical Science*, 1921, **5**, 24) in the infiltrations and in the capillaries. The writers point out that chancre of the cervix varies so greatly in its clinical aspect that a diagnosis can only be determined by removing a piece for microscopic examination. It is not enough to find *S. pallida* in smears, as the woman may be syphilitic and also have cancer. *S. pallida* may be present in the menstrual blood and in the genital secretions in the absence of local lesions.

Swayne found a positive Wassermann reaction in 30 per cent. of women with vaginal discharge but no symptoms of syphilis. The discharge ceased under antisyphilitic treatment. He thinks that the endometrium is subject to syphilitic lesions analogous to those of the mucous membranes.

Warthin gives details of post-mortem examination on a subject who died

from a fractured base two years after contracting syphilis, in which *syphilis of the prostate* was found. There were scars of former syphilitic ulcers on the skin, but no naked-eye changes in the organs. Microscopical examination, however, showed evidence of syphilis of the meninges, lungs, liver, suprarenals, testicles, and prostate, in the form of diffuse or circumscribed plasma-cell infiltrations, often perivascular, with proliferation of blood-vessels and fibroblastic tissue, often appearing as miliary granulomas, showing no caseation and with occasional giant cells. All these morbid changes were found in the prostate, and *S. pallida* was also demonstrated by the Levaditi method. There were no symptoms recorded during life pointing to any prostatic affection. The heart and aorta showed no signs of syphilis. Warthin claims this case to be the only one in which syphilis of the prostate has been absolutely demonstrated. His case is referred to in the series of 24 cases of alleged prostatic syphilis collected by Loyd Thompson (vide *Medical Science*, 1921, **3**, 298).

Burnier has collected 33 published cases of *syphilitic mastitis*, which show that this condition may occur at all stages of syphilis, and even in heredo-syphilis. Of the 33 cases, 10 occurred in the early secondary, 9 in the late secondary, 11 in the tertiary stage, and 3 in heredo-syphilis. Compared with gumma of the breast, syphilitic mastitis is more common in the secondary than in the tertiary stage, and is rather more frequent in women than men. It is generally unilateral, and appears to have no relation to the severity of the disease. Clinically, it appears in two forms; a diffuse infiltration of one or more lobes of the gland causing a hard diffuse swelling; or in the form of circumscribed nodules. The skin is generally unchanged, but sometimes adherent. In one case suppuration occurred. The axillary glands are sometimes enlarged. Syphilitic mastitis tends to resolve completely under treatment. It is important to diagnose it from cancer of the breast, especially as it is sometimes painful, immobile, adherent to the skin, and accompanied by enlarged axillary glands and retraction of the nipple. In such cases the therapeutic test is indicated.

Laederich and Tassin report a rare case of *symmetrical gummatous myositis* of the sternomastoid muscles, associated with periostitis of the manubrium in a woman aged 40. The patient presented a firm diffuse swelling occupying the region of the manubrium and extending for 5 or 6 cm. up both sternomastoid muscles. The skin was unaltered. There was no adenopathy. Other symptoms of syphilis were absent, and there was no history of infection, but the Wassermann reaction was positive, and the swelling disappeared under treatment by intravenous injections of cyanide of mercury and novarsenobenzol.

Lemierre and Weissenbach report two cases of syphilitic myositis affecting the muscles of the calf. The first case was one of subacute myositis commencing suddenly with pain and swelling of the middle third of the left calf, and occurring in the early secondary period in a woman aged 22. The second case was one of syphilitic gummata developing insidiously in the right gastrocnemius and peroneal muscles, in a woman aged 47. Both cases presented other obvious signs of syphilis and a positive Wassermann reaction, and both yielded to antisyphilitic treatment, by iodides and mercury in the first case and by neosalvarsan in the second. The authors mention that the calf-muscles are those most often affected by syphilitic myositis and after these the sternomastoid, according to cases collected from the literature by Lèfevre.

Rulison has investigated the presence of *epitrochlear adenopathy* in 252 cases of syphilis in all stages. He finds that one or both of the glands was enlarged in 79 per cent., including 66·6 per cent. in 42 cases of primary syphilis. In 43 non-syphilitic cases the gland was affected in 23 per cent. He concludes that enlargement of the epitrochlear gland is an early, persistent, and common sign of syphilis, but not pathognomonic, since it occurs in non-syphilitic cases; that it is an aid to diagnosis in the primary stage, when dark-field examination and the Wassermann reaction are negative; that in one-fifth of the cases the affection is unilateral; that treatment does not cause complete resolution; that it is less common in neurosyphilis, suggesting that those cases which develop neurosyphilis have less adenopathy.

Sabouraud has further investigated the syphilitic origin of *alopecia areata*. He finds that a positive Wassermann reaction occurs three times more often in cases of alopecia areata than in tinea tonsurans, and that deformities and malformations of the bones, genital organs, teeth and nails, and congenital heart disease are common in the subjects of alopecia areata. Although hereditary syphilis may not be the only cause of such malformations, the occurrence of several malformations in a subject is suggestive of hereditary syphilis, even if the Wassermann reaction is negative. The latter, as he remarks, tends to become negative as adolescence approaches. He finds that alopecia areata often occurs at the menopause in women and also in the subjects of exophthalmic goitre, and attributes this to the influence of the endocrine glands, which are often affected by syphilis. He concludes that hereditary syphilis is one of the principal causes of alopecia areata, but does not exclude other causes, such as reflex irritation due to late and difficult eruption of wisdom teeth (Jacquet), three cases of which he has observed. In fact, he regards the condition as a cutaneous reaction, which may be due to several causes. He mentions some cases cured by antisyphilitic treatment which had been stationary for years.

Leredde discusses the syphilitic origin of '*essential*' *epilepsy*, which was suggested by Fournier 30 years ago. He has collected 14 cases of essential epilepsy, six of which he regards as certainly syphilitic. Two of these had evidence of acquired and two of congenital syphilis, and the remaining two reacted to antisyphilitic treatment. He considers that most of the other cases were heredo-syphilitics, by the evidence of dental and other stigmata and by the history of syphilis in the parents or grandparents (transmission to third generation). It is noteworthy that in all but one of his cases the Wassermann reaction in the blood was negative, and Leredde points out that a negative reaction does not exclude syphilis as an aetiological factor in chronic affections any more than it excludes the presence of syphilis in individual infections. The frequency of the syphilitic serum reaction does not show the frequency of syphilis itself, which is always higher than that of the reaction. Leredde holds that the syphilitic origin of 'essential' epilepsy can be shown in most cases by careful investigation of the clinical evidence, and by the therapeutic test; and that, as epilepsy is a type of chronic affection in which the Wassermann reaction is usually negative, the evidence afforded by this reaction is of minor importance. The cerebrospinal fluid was tested by the Wassermann reaction in two cases only, one was positive the other negative.

Visceral syphilis. Allbutt draws attention to the frequency of *syphilitic ortitis* in the early stages of the disease. He quotes Turnbull's statistics of

60 autopsies on syphilitics, in which syphilitic affection of the aorta was found in 76 per cent. He reminds us that syphilitic aortitis often leads to aortic regurgitation, but not to stenosis, and that severance of a cusp of the aortic valve is characteristic of syphilis; that the prognosis of aortic regurgitation of syphilitic origin is bad, owing to frequent implication of the coronary arteries. Gibson points out that the early stages of syphilitic aortitis may often be revealed by radioscopy, which shows a blurred outline due to periarteritis. Other early signs mentioned by him are tenderness on pressure over the aortic area, pain after exertion due to stretching of the aorta, and paroxysmal tachycardia.

Concerning *cardiac syphilis*, Allbutt holds that there is no evidence of a diffuse myocarditis resulting in cardio-sclerosis except as an atrophic result of coronary occlusion. Cowan and Rennie, however, describe a case of diffuse myocarditis with newly-formed connective tissue, apparently of inflammatory origin and not dystrophic. A similar condition was found some time ago by Warthin in congenital syphilis. Cowan and Rennie remark that, as syphilis is rarely fatal in early years, its importance as a cause of cardiac affections is underestimated. The diagnosis is difficult and may depend on the history and presence of other signs; evidence is sometimes obtained by the discovery of ocular lesions. The Wassermann reaction may be negative. In 104 cases of aortic disease they found evidence of syphilis in 30·7 per cent., of acute rheumatism in 33·6 per cent.; the remaining 34·5 per cent. being of unknown origin. In nineteen aortic aneurysms evidence of syphilis was found in 63·1 per cent. On the other hand, in a series of cases of mitral disease 69·4 per cent. had had acute rheumatism, and only 0·8 could be attributed to syphilis. In auricular fibrillation, which is usually associated with mitral disease, syphilis was found in only 7 or 9 per cent., and in heart-block and myocarditis its incidence was slight. These observers conclude, therefore, that while aortic valvular disease is largely due to syphilis, mitral valvular disease rarely results from it. This conclusion apparently applies to acquired syphilis only; hence it is interesting to note that a positive Wassermann reaction was reported by Amblard in 128 out of 165 cases of mitral stenosis, together with frequent signs or history of congenital syphilis.

As regards *pulmonary syphilis*, Allbutt remarks that syphilis may affect the apex of the lung and undergo caseation, simulating tuberculosis; that it tends to affect the root of the lung and spread along the bronchial tubes, when it may also be difficult to distinguish from tubercle by radioscopy; that it may lead to compensatory emphysema and bronchiectasis by the formation of scar-tissue; lastly, that *S. pallida* and the tubercle bacillus may co-exist. Benoit regards pulmonary syphilis as rare. He mentions that Osler only found 12 instances of lung syphilis, 8 of which were in hereditary syphilitics, in 2,800 autopsies, and Symmers only 12 in 314 cases of syphilis found in 4,880 autopsies. On the other hand, cases diagnosed as advanced pulmonary tuberculosis have been cured by salvarsan, mercury, and iodides. The symptoms in such cases are those of phthisis. Diagnosis depends upon repeated negative findings for the tubercle bacillus, X-ray examination and the effect of antisyphilitic treatment. If the apices are free, and the signs are localized to the base or hilus of the lung, the presumption is in favour of tumour or syphilis. Again, the two diseases, syphilis and tubercle, may co-exist; a syphilitic subject may be infected with tubercle and show both a positive Wassermann reaction and the presence of tubercle

bacilli. In such cases intensive treatment for syphilis should be given, as syphilis aggravates the tubercular process. Benoit recommends six weekly injections of arsenobenzol in progressively increasing doses, then mercurial inunctions, and iodides : this course to be repeated if the Wassermann reaction remains positive. According to Minton, syphilis of the apex of the lung is not infrequent, and is often mistaken for pulmonary tuberculosis. He mentions five cases reported by Landis and Lewis and describes three cases of his own, all occurring in the same dispensary. Collectively, these patients presented the principal signs of tuberculosis—prolonged cough, blood-stained sputum, night sweats, dyspnoea, gastric disturbance, loss of weight, curvature of the nails, slight elevation of temperature and increased pulse-rate, flat chest, impaired resonance over apices, bronchial breathing, increased vocal resonance, and râles. On the other hand, the sputum was negative for tubercle bacilli, and the Wassermann reaction was strongly positive in all three cases. The pulmonary symptoms were greatly relieved by antisyphilitic treatment. This consisted of salvarsan injections followed by mercury and iodide in one case, mercury and iodide alone in the second case ; in the third case the nature of the treatment is not stated.

Stimson describes three cases of syphilis of the *trachea and bronchi.* The first case, a woman aged 30, suffered from paroxysmal cough, stridor, and dyspnoea; there were no signs or history of syphilis, but the Wassermann reaction was strongly positive. No signs of aneurysm or mediastinal growth were found and a diagnosis was made of syphilis of the left bronchus, with obstruction. Symptoms were relieved by mercury and 0·3 gm. salvarsan, but death took place from exhaustion. The autopsy revealed gumma of the bronchi with stenosis of left bronchus, gumma of liver, chronic parenchymatous nephritis, and lobar pneumonia. The second case, a man aged 40, also suffered from paroxysmal, cough, stridor, and dyspnoea ; there was no syphilitic history. The Wassermann reaction was strongly positive. Bronchoscopy revealed a papule formed of chronic inflammatory tissue. Syphilis of the trachea was diagnosed. The symptoms were much improved by arsenobenzol and mercury. The third case, a woman aged 33, suffered from severe dyspnoea. No history of syphilis, but Wassermann reaction positive. The patient died, and there was no autopsy. Diagnosis, syphilis of the right bronchus. The author sums up that the characteristic symptoms of syphilis of the trachea and bronchi are those of obstruction, manifested by dyspnoea with prolonged inspiration ; paroxysms of excessive dyspnoea which may be fatal ; a hard, brassy, and paroxysmal cough, and stridor. Other symptoms may be more or less profuse expectoration and limitation of movement of the larynx, but wide variations in the symptoms are not uncommon.

Chiray and Janet report a case of syphilitic *pleuro-peritonitis* in a woman aged 36. The symptoms commenced with fever and vomiting and variable abdominal pains, at first suggesting appendicitis or cholecystitis. Later on signs of dry pleurisy appeared and the temperature remained at 38° C. for two months, suggesting tuberculous pleuro-peritonitis. The diagnosis was cleared up by the appearance of syphilitic periostitis of the skull and clavicle and a positive Wassermann reaction. After three injections of neosalvarsan the pleuro-peritoneal symptoms subsided as well as the periostitis, and the patient made a good recovery. Chiray remarks that this case shows that the pleuro-peritoneal syndrome, normally attributed to tuberculosis, may be produced by syphilis, and that there may be a tertiary

syphilitic pleurisy. The onset, with sub-hepatic pains, may give rise to erroneous diagnosis. This case is also another example of fever associated with visceral syphilis, an occurrence too often ignored.

In addition to the more usual forms of *hepatic syphilis*, a febrile hypertrophic form is described by Gilbert, Chiray, and Alfred-Coury in connexion with tertiary syphilis. This is characterized by fever lasting for months or years, considerable enlargement of the liver, variable enlargement of the spleen, absence of jaundice and functional hepatic disorders, and remarkable response to antisyphilitic treatment, both mercurial and arsenical. This condition is important as regards diagnosis, for it may be mistaken for tuberculosis, amoebic dysentery, malaria, or even cholecystitis. Notes are given of four illustrative cases. The authors remark that visceral syphilis is often febrile, and that tertiary syphilitic fever is particularly resistant to antifebrile remedies, but rapidly subsides under antisyphilitic treatment. Mayer has investigated the syphilitic factor in all cases of *acute yellow atrophy* of the liver which were observed in the Rudolf-Virchow Hospital, Berlin, between January 1919 and April 1921, cases due to phosphorus and other poisons being excluded. There were 25 typical cases, 13 females and 12 males. The age was in most of them between 20 and 30 years, but one case was aged 56, and another 10 years, a boy with hereditary syphilis. There was definite evidence of syphilis in 15, probable evidence of syphilis in 5, no evidence in 2, and 3 occurred in pregnant women. Mayer regards syphilis as a constant factor, and suspects its presence in the pregnant women and in the two cases in which no evidence was apparent. However, he thinks that another factor must be necessary, owing to the rarity of the condition, and that the second factor is probably biliary infection.

A remarkable case of *gastro-hepatic syphiloma* is reported by Florand and Girault in a man aged 45, who had suffered from abdominal pain for three years and repeated vomiting for upwards of a year. A tumour, the size of a small orange, was felt in the pyloric area; the liver and spleen were apparently normal; there was a history of chancre 27 years previously, and the Wassermann reaction was weakly positive. Radioscopic examination showed the presence of a tumour causing dilatation of the third part of the duodenum. Under treatment with neosalvarsan, injections of mercuric cyanide, and potassium iodide the pain and vomiting ceased. A second X-ray examination showed that the dilatation of the duodenum had subsided, but not the tumour. Laparotomy was then performed and revealed a lobulated tumour in the left lobe of the liver, firmly fixed to a second tumour in the pyloric region; the latter being smooth, not ulcerated, and not circumferential. Gastro-enterostomy was performed. Mercurial injections were resumed after the operation, and in five weeks the tumour had apparently disappeared. The diagnosis of syphilis was based on the mobility and clearness of outline of the tumour under X-ray examination, the absence of cachexia, the tolerance of iodides, and the history of former syphilis. The authors remark on the absence of clinical signs pointing to the liver, and mention that the union of the two tumours prevented excision.

Tallquist's clinical and post-mortem investigations suggest that the orthodox text-book view as to the frequency of tertiary syphilis of the liver requires revision. Among 2,117 necropsies carried out in Helsingfors in the 10-year period, 1910–19, syphilis of the liver in adults was found only in 7 men and 1 woman. In none of these cases had this condition been detected by the clinician, and it may, therefore, be supposed that it is often overlooked

during life. It is also conceivable that gummata of the liver may heal so completely as to escape detection *post mortem*. Tallquist calculates that during 25 years' practice, and among 24,433 patients, only a few of whom were children, about 3 per cent. were syphilitic. There were 16 men and 12 women in whom the diagnosis of tertiary syphilis of the liver could be regarded as practically certain. In addition to these hospital cases, there were 6 men and 1 woman seen in private practice with signs of late syphilitic hepatitis. Thus only 0·06 per cent. of his 11,000 patients in private practice showed clinical signs of tertiary syphilis of the liver. If the incidence of this condition in hospital practice be estimated at 0·12 per cent., it is only about one-third of its incidence in the dead-house. The average length of the period between infection and the outbreak of this condition in these 35 cases was 18 years; the shortest interval was 3 years, the longest 22 years. A striking feature of these cases was the inadequacy of the specific treatment they had received; 10 of them had, indeed, received none.

Another observation was that tertiary syphilis of the liver and syphilis of the nervous system hardly ever occurred simultaneously. In fact, this coincidence was noted only in 1 out of the 35 clinical and 8 post-mortem cases. The explanation may be that syphilis of the nervous system is, comparatively speaking, an early sequel to infection. With regard to diagnosis, 18 of the most recent cases were controlled by the Wassermann reaction, which was positive in 17. Enlargement of the liver was found in 75 per cent., spontaneous pain in 50 per cent., ascites in 28·5 per cent., jaundice in 20 per cent., and fever in 50 per cent. If a recent history of fever in patients, afebrile at the time of examination, be correlated with the syphilitic hepatitis, then fever is a common accompaniment to this condition and is a useful guide to it. Tallquist is optimistic as to the results of vigorous specific treatment; among the 20 cases treated since 1910 and exhibiting no complications, 7 were discharged as cured, and 11 as improved in consequence of specific treatment.

Syphilis of the *pancreas*, according to Wile (1), is common in congenital, but rare in acquired syphilis. The clinical features he mentions as suggestive of syphilis are jaundice, glycosuria, and the formation of a tumour without cachexia. Warthin, however, who found syphilitic lesions in six autopsies on diabetics in whom syphilis was unsuspected during life, regards interstitial pancreatitis as common in latent syphilis and a cause of diabetes.

Wile (2) regards enlargement of the *spleen* as common in early secondary syphilis, when it is coincident with the general lymphadenitis. He and Elliot found the spleen enlarged in 36 per cent. of their cases, by palpation alone. As a rule, there are no symptoms, but occasionally pain is present. Under treatment the swelling subsides, but in untreated cases, according to Wile, the spleen may remain permanently enlarged, develop chronic interstitial splenitis, and form a depôt for spirochaetes. In late syphilis, interstitial, parenchymatous, and gummatous splenitis may occur, but are rare and usually associated with syphilis of the liver, kidneys, or other viscera.

Pinard, investigating the history of 23 cases of *diabetes*, found that 10 showed evidence of old acquired syphilis and 5 of hereditary syphilis; of the remaining 8 no inquiry for syphilis had been made. He mentions cases in which sugar disappeared in the urine during treatment with salvarsan and reappeared afterwards. He also mentions that Warthin found syphilitic lesions in six cases of diabetes, although they were unsuspected during life. Pinard concludes that syphilis, acquired or hereditary, is an

important cause of diabetes, which may be due to pancreatic, hepatic, hypophyseal, or bulbar lesions, and that syphilitic diabetes may be benefited by antisyphilitic treatment. Other observers, however, find evidence of syphilis in a smaller percentage of cases of diabetes. Thus Rosenbloom, in 139 cases of diabetes mellitus found a positive Wassermann reaction in about 12 per cent. Intensive treatment had no effect in increasing tolerance for carbohydrates. He concludes that in about 6 per cent. the diabetes was syphilitic in origin, and in about 6 per cent. independent of syphilis. He quotes other observers as having obtained similar percentages.

Diagnosis. The final part of an *inquiry into the Wassermann reaction*, held by the *Annales des Maladies Vénériennes*, deals with the results of the reaction compared with clinical evidence. The main questions discussed are: (1) the occurrence of positive reactions in the blood or cerebrospinal fluid in non-syphilitic subjects; (2) the percentages of positive reactions in the different stages of syphilis; (3) the significance of reactivation, or provocative injection; (4) the value in prognosis and treatment.

With regard to the occurrence of positive reactions in non-syphilitics, Gougerot, from an experience of 6,957 reactions in non-syphilitic subjects, obtained only 21, or 0·45 per cent., of positive reactions, using three parallel methods; the original Wassermann technique modified, Desmoulières' method with antigen of cholesterinized heredo-syphilitic liver, and a modified form of Hecht's method. In leprosy he found weak positive reactions in some cases, and in others—clinically similar—negative reactions, and suspects that the former were also infected with syphilis. In malaria he observed weak positive reactions which disappeared after treatment with quinine, and would suspect associated syphilis in the case of a strong positive reaction.

Bory found positive reactions during the acute periods of scarlet fever, measles, and erysipelas, also in Vincent's angina, enteric fever, epidemic cerebrospinal meningitis and ictero-spirochaetosis. These reactions were weak with most antigens, but more strongly positive with cholesterinized antigen. Emery and Morin, on the other hand, using both the Wassermann and Hecht techniques, did not obtain any positive reactions in leprosy, malaria, or acute fevers. Concerning the cerebrospinal fluid, Ravaut observed one case of cerebrospinal meningitis in which a positive reaction was obtained, and Oltramare states that in 20 out of 31 cases of meningitis, diagnosed as tuberculous or influenzal, he obtained positive reactions; but the replies of all other observers to this question were in the negative. The result of this part of the inquiry may be summed up in the words of Gougerot: 'Apart from yaws and leprosy, no diseases which can be confounded with syphilis cause fixation of complement with heredo-syphilitic liver, provided slight fixations are counted as negative. We can therefore conclude that, apart from acute diseases, profound cachexia, and exceptional chronic diseases (yaws, leprosy), a positive Wassermann reaction indicates a diagnosis of syphilis.'

As regards the percentages of positive reactions in active syphilis, most observers found from 90 to 100 in secondary syphilis and 50 to 90 in tertiary syphilis. In tabes, Sicard found the blood positive in 75 and the cerebrospinal fluid positive in 98 per cent., in classical cases with ataxia; in non-ataxic cases, his figures are 70 and 80, and in general paralysis 97 and 100 respectively.

Most observers agreed that the date of first appearance of a positive

reaction varies considerably; Gougerot gives from 15 to 120 days in untreated cases, as distinguished from retardation due to treatment; others give from 15 to 30 days after the chancre with the usual technique, earlier with Hecht's method. In ocular syphilis Morax mentions that a positive reaction is much more frequent in corneal than in retinal and choroidal lesions. In hereditary syphilis Gougerot gives 96 as the percentage of positives in cases with actual lesions. According to Sabouraud, all heredo-syphilitics with actual lesions give a positive reaction, and most children with dental abnormalities, but the percentage of positive reactions diminishes as age increases. Weil mentioned 15 cases under 18 months of age with visceral and nervous syphilis which gave a negative reaction, 7 of these having meningitis which was cured by antisyphilitic treatment. Opinions differed as to the method and the value of reactivation, or provocative injection; Gougerot and others attached considerable importance to this test in old syphilitics as a guide to prognosis and treatment; but Dujardin held that absence of reactivation does not necessarily mean a cure, and Ravaut doubted the specificity of the reaction. There were also differences of opinion as to the value of the reaction in prognosis and treatment. Carle held that regular and thorough treatment should be continued for two or three years whatever the results of the reaction, and pointed out that tertiary or nervous lesions may appear after the reaction has been negative for some years. Ravaut regarded it as dangerous to give the reaction too great a rôle in the direction of treatment; while an attempt should be made to render the reaction negative and maintain it so, the attainment of this result is not a sufficient indication of cure or for suspension of treatment; in old syphilitics it is sometimes impossible to reduce the reaction. With regard to irreducible reactions, Gougerot said there is often an unsuspected focus of disease, and advised lumbar puncture and radioscopy of the aorta. The inquiry terminates by emphasizing the dangers of tests performed by others than competent serologists, and by urging greater uniformity in methods and standardization of technique.

Standardization of the different reagents concerned in the Wassermann reaction forms the subject of a long series of articles by Kolmer in the *American Journal of Syphilis.*

Levinson reviews the various *precipitation and flocculation reactions* which have been devised to supplant the Wassermann reaction and simplify the serum diagnosis of syphilis, more especially the Sachs-Georgi and Meinicke reactions. He remarks that there are two schools of thought; one which believes that the Wassermann reaction is an antigen-antibody reaction, and attempts to modify and simplify this reaction; another which attempts to show a parallelism between the Wassermann and certain colloidal reactions. The latter has led to the Sachs-Georgi and Meinicke reactions. From his own observations Levinson found that while the Meinicke reaction agreed with the Wassermann in 88·8 per cent., the Sachs-Georgi agreed in 92 per cent., so that the advantage lies with the latter reaction, which is also the simplest. In spinal fluid examination in cases of neurosyphilis Levinson found agreement between the Wassermann reaction and Sachs-Georgi tests in 79 per cent. The Sachs-Georgi reaction was positive in a larger number of clinically positive cases of syphilis than the Wassermann reaction. It became positive earlier and remained positive longer than the Wassermann. It was not influenced by treatment to the extent of becoming negative after one or two injections of salvarsan, and it was found in congenital syphilis and in latent syphilis. However, Levinson is of opinion that at present the

Wassermann reaction should be supplemented and not supplanted by the Sachs-Georgi reaction, and that the various factors causing flocculation require further investigation.

Taniguchi and Yoshimare have compared the *Sachs-Georgi test* with the Wassermann reaction in 1,575 cases, including cases from a general hospital as well as from a venereal clinic. The results agreed in 90 per cent. Of the 10 per cent. discrepancies, comprising 157 cases, the Wassermann reaction was positive and the Sachs-Georgi test negative or doubtful in 23, the converse in 77. The Sachs-Georgi test, therefore, gave more positive reactions. In treated cases this test also gave a higher proportion of positives, the agreements with the Wassermann reaction being 81 per cent., the discrepancies 19 per cent. Human heart cholesterol antigen was used for the Wassermann reaction.

Harryman has applied the Sachs-Georgi test to the cerebrospinal fluid in 379 cases, the majority of which were cases of general paralysis, tabes, and cerebrospinal syphilis, the remainder cases of primary, secondary, tertiary, and latent syphilis. He found absolute agreement with the Wassermann reaction in 85 per cent. and 95 per cent. if doubtful results or weak reactions were excluded. He thinks the Sachs-Georgi test more sensitive and capable of giving earlier diagnosis in syphilis of the central nervous system.

Dreyer has lately devised a modification of the Sachs-Georgi reaction by which he claims that quantitative results can be obtained. He points out that the Wassermann test, besides being complicated, is not really quantitative, so that the results of different workers are difficult to compare. The Herman-Perutz test, introduced to avoid the necessity of using a haemolytic system, and depending on the production of flocculation by adding syphilitic serum to a saline suspension of sodium glycocholate and cholesterin, has proved less sensitive than the Wassermann reaction and gives false positives. Sachs and Georgi improved the flocculation test by using an alcoholic heart extract with cholesterin, but this test also gives false negatives and false positives. In Dreyer's modification the reagents are similar to those of Sachs and Georgi, viz. an alcoholic extract of calf's heart, a 1 per cent. solution of pure cholesterin in absolute alcohol, and sterile 0·9 per cent. saline. Dreyer remarks that in such a test there should be only one variant—the serum to be tested; that the results should be expressed in definite units per cubic centimetre of the different reagents used in the test, and that the standard unit should be easily maintained and checked. The 'standard' flocculation is that which can be seen with the naked eye, a 'trace' of flocculation being only seen with a lens. For details of technique the original article should be consulted. Dreyer's results compared with the Wassermann reaction are as follows. In 1,072 cases with definite evidence of syphilis the results agreed in 1,008 (94 per cent.). In the remaining 64 cases the Wassermann reaction was negative and the Sachs-Georgi test positive in 59, and the converse in 5 cases. In 5 cases with no definite evidence of syphilis the Wassermann reaction was positive and the Sachs-Georgi test negative in 4, and the converse in 1 case. Dreyer claims that with his test the results are quantitative as well as qualitative; that the reaction can be standardized, and the results of different workers compared; that the results of treatment can be followed and different methods of treatment compared by their effect on the reaction.

Okell has compared the Wassermann reaction with the original Sachs-Georgi reaction and with Dreyer's modification. He finds that the latter

agrees with the Wassermann reaction in 97 per cent. and the original in 90 per cent.

Discussing the best course to pursue when a patient, who happens to be in hospital, proves to be syphilitic, Faber draws special attention to the cases in which a positive Wassermann reaction is the only evidence of syphilis. In section B of the Bispebjaerg Hospital a Wassermann survey of 1,356 of its inmates showed that 9·1 per cent. were syphilitic. Among these cases were 24 in which a positive Wassermann reaction was the only sign of syphilis. Ought they to have been given specific treatment, and, if so, ought such treatment to have been pushed vigorously? With regard to the latter question, Faber is still uncertain, but he answers the first question emphatically in favour of specific treatment on the following evidence. Six years after these patients' discharge he succeeded in tracing and re-examining 9 of them. All these 9 still showed a positive Wassermann reaction, 1 had developed early aneurysm of the aorta, and 3 showed sensory disturbances of the feet. In 1 case there were signs of early tabes.

Prophylaxis. Schumacher discusses the practical value and mode of action of venereal prophylactics. Of the prophylactic preparations used against syphilis, the one in most common use—Metchnikoff's calomel ointment—he regards as the least valuable. The reasons given for this opinion are that calomel is insoluble, and that the disinfecting action of mercurial preparations depends on the action of free mercury ions, which are only found when the mercurial salt is in solution. Any disinfecting power possessed by calomel ointment must, according to Schumacher, be due to the presence of soluble mercurial salts as impurities in the calomel. Hence, mercurial prophylactics must be in solution. Neisser's mixture of perchloride of mercury with gelatin, starch, and tragacanth is good if used fresh, but must be dispensed in glass or porcelain tubes, as metal tubes cause precipitation of the mercury. Oxycyanide of mercury, however, according to Schumacher, is useless, as its solution forms no mercury ions. As regards the mode of application of the prophylactic, solutions appear to be preferable to ointments. Manteuffel found a 0·1 per cent. solution of perchloride of mercury more successful than an ointment of the same strength. After eight years' experience with sublimate prophylaxis Schumacher concludes that thorough washing of the penis and urethral orifice with perchloride of mercury solution is the best prophylactic against syphilis. Next to this he places quinine ointment, although he has had no experience with it. Neisser's sublimate preparation he places third in value.

Treatment. Delavenne has compared the results of *pure arsenical treatment* of syphilis with *treatment by mercury and arsenic*. From an experience with 105 cases observed during five years he comes to the following conclusions: (1) The effect of pure arsenical treatment appears to be distinctly inferior to combined mercurial and arsenical treatment, both as regards its permanent effect on the Wassermann reaction and its therapeutic stability; (2) the cicatrizing power of '914' is in most cases rapid, but sometimes fails, and cases resistant to arsenic are comparatively frequent; (3) the numerous clinical and serological relapses during the first years of syphilis show that prolonged treatment with serological and clinical observation is necessary; (4) from the social point of view, pure arsenical treatment presents serious drawbacks, owing to the recrudescences of the disease due to irregular and insufficient treatment. The arsenical preparation used was neosalvarsan, given in weekly injections to a total of

3 or 4 gm.; the mercurial treatment was by intravenous injections of cyanide of mercury or intramuscular injections of benzoate up to twenty injections.

Chargin has compared the results obtained by the three following forms of *intensive treatment*, as judged by the Wassermann reaction: (1) Pollitzer's method of three intravenous injections of full doses of arsphenamine given on three successive days, followed by six weekly mercurial injections of either insoluble salicylate or mercurial oil in doses up to 2 gr., and finally three more injections of arsphenamine given either on three successive days or weekly. This is the more intensive type of treatment. (2) Three or four arsphenamine injections given on alternate days, followed by 6 mercurial injections, and then by 3 to 5 more of arsphenamine given weekly or on alternate days. This is another intensive plan. (3) Alternate courses of 6 to 8 injections of arsphenamine, and 10 to 12 of mercury. The arsphenamine injections were given at intervals of 5 to 7 days and the mercury between them. This is a less intensive method, the average doses being 0·35 gm. for females and 0·4 for males. The cases treated were all recent infections, 37 being treated by the first method, 19 by the second, and 50 by the third. The Wassermann reaction became negative by the 10th week in 80 per cent., and all were negative by the 20th week. As the serological and clinical results were practically the same by all methods, Chargin concludes in favour of the third, or less intensive plan, which is safer.

Fraser considers that the proper way to administer arsenobenzene is by intramuscular or subcutaneous injections, so that its absorption may be gradual. The preparation he prefers is sulfarsenol, administered subcutaneously over a long period, combined with mercury, and also intramine, which he believes has a protective action for the nervous system. By this means, he holds that the drugs find their way into the intrathecal system and do not tend to produce a sudden systemic sterilization with consequent destruction of the antibody supply. He blames the modern intensive treatment as being responsible for the increasing incidence of early neurosyphilis. This increase he considers to be well established by the evidence, and that it is due to the deprivation of the central nervous system of its antibody supply by rapid sterilization of the general system. The defects of the modern intensive system of treatment are, he holds, as follows: (1) the tendency to treat primary syphilis *en masse*; (2) the method of working to a mechanical time-table; (3) the blindfold method of working for a negative Wassermann reaction ('the syphilologist is being strangled by the tyranny of the Wassermann reaction'); (4) failure to interpret pathological findings in the light of the clinical picture. The nervous system, he remarks, is invaded during the period of early generalization, and the nervous involvement may be symptomatic or asymptomatic. In the absence of clinical signs a normal spinal fluid may indicate the successful resistance of the central nervous system to the virus or failure to react. A pathological spinal fluid may indicate implication or protective power, which cannot be distinguished in the absence of symptoms. The occurrence of neurosyphilis is influenced by the patient's power of resistance; the natural resistance of the central nervous system and its inherent capacity for producing antibody; the stage at which treatment is commenced; the method employed and the duration; the type of *S. pallida* which caused the infection, connected with which is the question of a life-cycle. Treatment, he concludes, should aim at conserving sufficient antibody for the protection of the central nervous

system, instead of leaving it defenceless by rapid sterilization of the systemic circulation. Each case should be treated on its merits instead of as one of a series. Pathological findings should be carefully correlated with clinical observation.

Kilroy gives the results of eighteen months' experience with the *intramuscular injection of novarsenobillon* and sulfarsenol. The course of novarsenobillon consisted of eight injections at fourteen-day intervals, six doses of 0·45 gm. and two doses of 0·6 gm.; that for sulfarsenol six doses of 0·4 gm. to 0·48 gm. and two doses of 0·6 gm. The intramuscular route has the advantage of slow absorption. Mercury was given by the mouth as the buttocks were used for the arsenical preparations. The cases treated comprised 15 primary, 6 secondary, and 25 older cases of syphilis. A negative Wassermann reaction was obtained after treatment in all the primary cases, in all but one of the secondary cases, and in 16 out of the 25 older cases.

Duroeux concludes that *sulfarsenol* is one of the most active of the arsenical compounds, equal in action to salvarsan and superior to neosalvarsan, and that the Wassermann and Hecht reactions are rapidly transformed to negative, and remain negative for longer periods than with neosalvarsan. He holds that the curative action of the arsenical compounds depends less on the quantity of the drug administered than on the frequency of injections, and, therefore, that progressively increasing doses should be given at short intervals. In one series of primary and secondary syphilis he gave intravenous injections of 12, 18, 24, 30, 36, 42, 48, 54, and 60 cgm., a total of 3·24 gm. The first three injections were given every two days, the rest at intervals of three days. Five days after this course the Wassermann and Hecht's reactions were negative. A second course was given after an interval of 12 days, and further courses every other month, the total duration of treatment being 16 months. After this the blood reaction remained negative. In another series of cases he gave weekly injections. Comparison of the two methods showed that in the first series (124 patients) the blood became negative after the first course in 87 per cent., while in the second series (162 patients) it became negative in 68 per cent. The minimum time to produce a negative reaction was from 18 to 22 days after commencing treatment. In five cases of primary syphilis with negative reaction he thinks he obtained an abortive cure with 10 intravenous injections in doses from 6 to 60 cgm. The dates of the chancres were from 3 to 25 days and the cases remained negative, after provocative injection, while under observation for periods of 8 to 14 months. In neurosyphilis Duroeux found that sulfarsenol was beneficial, but had not enough cases to form a conclusion. In these cases he prefers subcutaneous injection.

Walson reports on the treatment of 800 cases of syphilis by *silver-salvarsan*. From this experience he concludes: (1) that silver-salvarsan is the strongest spirochacticide and the least toxic of all the arsenobenzol preparations; (2) that its effect on all clinical manifestations of syphilis is as rapid and effective as that of any of the other preparations; (3) that mercury should be given, either simultaneously or after silver-salvarsan. The doses he recommends commence with 0·1 gm., increased to 0·2 gm. for women and 0·25 for men, given intravenously at intervals of four days. Not more than 2 gm. should be given in one month. No alarming after-effects occurred in his cases, and there were only two cases which could be called arsenical poisoning. In one of these vertigo, vomiting, epigastric pain,

diffuse erythema, and slight jaundice occurred after the third dose. In the other case diffuse erythema, jaundice, and albuminuria occurred after the seventh dose. Walson points out that care is required in the administration of silver-salvarsan, as its dark colour renders it difficult to ascertain if the drug is completely dissolved. Freshly distilled water is used for solution, in the proportion of 10 c.cm. for each 0·1 gm. of the drug.

Boas has treated 315 cases in every stage of syphilis with intravenous injections of silver-salvarsan, each patient receiving, as a rule, four injections, the doses being respectively 15, 20, 25, and 25 cgm. His belief in the efficacy of silver-salvarsan was not profound enough to make him dispense with simultaneous treatment with mercury. Fever was a fairly common sequel to the injections, the symptomatic effect of which was usually prompt. He found the drug quite as beneficial as old salvarsan given by intramuscular injection, and within 24 hours of an intravenous injection of silver-salvarsan there was a complete disappearance of the spirochaetes. Though he did not feel justified in abandoning mercurial treatment, Boas considers that silver-salvarsan alone acts just as effectively as the combined treatment with mercury and salvarsan. In several cases silver-salvarsan was given by itself so as to obtain a clear impression of its efficacy, treatment with mercury being deferred till the completion of the course of silver-salvarsan. Undoubtedly intravenous injections of silver-salvarsan are more potent than intravenous injections of '606'. In addition to its antisyphilitic properties, silver-salvarsan has a certain tonic effect, and all the patients treated by Boas gained weight rapidly. Herxheimer's reaction was seen in several cases. Boas tabulates his material according to the stage of the disease and the behaviour of the Wassermann reaction. Of the 28 cases of primary syphilis with a negative reaction at the beginning of treatment, all continued to give a negative reaction, and all of the 10 cases of primary syphilis with a positive reaction at the beginning of treatment showed a negative reaction on its completion. All the 59 cases of secondary syphilis gave a positive reaction at the beginning of treatment, but only in 2 cases was it positive after treatment. Of 117 patients observed for a period of 3 to 18 months, only 3 showed signs of relapse. Boas concludes that silver-salvarsan is at least as effective as old salvarsan in controlling the manifestations of syphilis, and as the former is much more soluble, it is preferable to the latter, always provided the former's reputation for permanent effects is maintained.

Bodin has investigated the occurrence of *icterus after treatment by novarsenobenzol*. For this purpose he treated three series of cases numbering 254, 113, and 472 respectively, with novarsenobenzol from three different sources. No other treatment was given. The cases were mostly primary and secondary syphilis, but cases of latent syphilis and tabes were included in each series. In the first series there were two cases of icterus both in primary syphilis. In the second series there were also two cases, one in secondary syphilis, the other in latent syphilis. In the third series there were 34 cases of icterus, 23 in secondary syphilis, 9 in latent syphilis, and 2 in tabes. The percentages of the three series were 0·78, 1·7, and 7. The jaundice occurred after a single course of injections 19 times; after a second course 13 times; after a third course 6 times; and after a fourth course 6 times. Sometimes it appeared during the course of treatment, sometimes from one to ten weeks after completion of the course. As most of the cases occurred in the third series, Bodin concludes that icterus occurring after treatment with arsenobenzol is due chiefly to defects in preparation of the drug. He thinks the

amount of the drug administered is also a factor, because, in the first series, with the lowest percentage of icterus, the total of novarsenobenzol injected was from 2·5 to 3 gm., while in the other two series, with higher percentages of icterus, it was from 4 to 5 gm.

Two cases of icterus following injection of novarsenobenzol are reported by Arnozan, Petges and Damade, and Bousquet and Petges. The first case, occurring after a third injection of 0·45 gm. was preceded by a severe nitritoid crisis and terminated fatally a week after the injection. The autopsy showed old fatty degeneration of the liver and signs of old tubercle in the lungs. The second case occurred fifteen days after the last of a series of injections (0·30, 0·45, 0·60 gm.) and was accompanied by general oedema, ascites, and oliguria. All symptoms disappeared after treatment by injections of benzoate of mercury. The first case was apparently due to arsenical intoxication and the second was syphilitic in nature.

The guarded conclusions to which Åhman has come with regard to the marriage and progeny of persons who have undergone abortive treatment for early syphilis are founded on fourteen cases, and a prolonged clinical and serological observation of both parents and progeny. In seven of his nine male cases the Wassermann reaction had not become positive when specific treatment was instituted (a combination of salvarsan and mercury) and it never became positive, although clinical and serological supervision was maintained for many years. But two of these patients had infected their wives before treatment was instituted, and these two women were, therefore, also given specific abortive treatment. After giving details of isolated cases, Åhman sums up thus: 'It is particularly important for prospective mothers, suffering from syphilis, to undergo thorough treatment, and in giving his consent to marriage the physician should be more rigorous in his standards in the case of women than in that of men. Even when there has been no serological evidence of syphilis at the time of institution of thorough specific abortive treatment, it is still advisable to demand an observation period of two years (clinical and serological) before consent is given to marriage. If the success of abortive treatment is proven in a longer series of cases than are yet available, a reduction may be made in this two-year observation period; but as long as isolated cases of relapse occur, even under apparently ideal conditions for early and complete abortive treatment, it is unwise to relax the two-year standard.'

Almkvist has weighed daily patients undergoing antisyphilitic treatment, and his observations refer to 368 separate courses of treatment. These included 20 courses of mercury alone, 132 of salvarsan alone, and 216 courses of mercury and salvarsan, the salvarsan in most of these cases being given before the mercury. The usual effects of the two drugs on the body-weight were opposite; salvarsan was associated with a daily rise of weight averaging 50 to 200 gm. in 72 per cent., whereas mercury provoked a daily loss of weight in 67 per cent. of the cases treated. This daily loss ranged from 50 to 200 gm. It depended largely on the dosage; if this was increased, the loss of weight became more rapid, and it slowed down again when the dosage of mercury was reduced. Although loss of weight was sometimes accompanied by other signs of mercurial poisoning, this was not invariably the case, and even rapid loss of weight might be unaccompanied by any other sign of mercurial poisoning. As the tolerance of the individual to mercury varies greatly, and the dosage cannot therefore be stereotyped, it is important to control it by frequent weighing. Small doses should be given at first, and

the amount gradually raised just short of the loss of weight limit and other signs of mercurial poisoning. The reaction of the body-weight to salvarsan also shows wide differences in the tolerance of the individual, and in some cases a gain of weight observed during the first stage of a course of salvarsan may be followed by a loss when the dosage of salvarsan is pushed beyond a certain limit. Almkvist does not regard the gain of weight following salvarsan treatment as a danger signal, but he admits that the processes leading to the gains and losses of weight from salvarsan treatment are still obscure.

Sazerac and Levaditi have tried the effect of *bismuth* in the experimental syphilis of rabbits. The animals were inoculated with virus from human chancre ('dermotropic') and from a case of general paralysis ('neurotropic'). The preparation used was tartrobismuthate of potassium and sodium, administered subcutaneously or intramuscularly in aqueous solution, in doses of 0·100 gm. per kilo body-weight. The cutaneous lesions healed rapidly in animals inoculated with either virus. This form of treatment has been tried in the human subject by Fournier and Guénot, who used an oily suspension of the drug, administered by intramuscular injection. A total of 2 to 2·50 gm. was given in the course of three or four weeks; at first in doses of 0·20 gm. every other day or 0·30 gm. every third day, the intervals being increased with later injections. The number of patients treated was 110, including all stages of syphilis. Chancres and mucous syphilides are said to have healed after one or two injections, and a case of palmar syphilide in fifteen days. Rapid effects are also reported in tertiary lesions, meningitis, and some improvement in leucoplakia. The Wassermann reaction was attenuated after the first series of injections, but further observation is necessary to determine the eventual result. The only accident liable to occur from bismuth is stomatitis, which resembles that produced by mercury, but is less severe. Bernard also reports favourably on the bismuth treatment, especially in cases intolerant of arsenic or mercury.

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C. F. M.
C. L.

ABSTRACTS

SURGERY

Nieden, H. Beitrag zur Aetiologie der akuten Magenlähmung. [**Contribution to the aetiology of acute dilatation of the stomach.**] *Arch. f. klin. Chir.*, 1921, **117**, 338–422.

The author has used the rate of emptying of the stomach as determined by X-ray examination after a barium meal as an index of the damage to the functions of the stomach produced by various experimental procedures, using dogs as the subjects. After excluding ether anaesthesia as a cause of delay in the time of emptying, he cut both vagi below the diaphragm and got the well-known dilatation effect on the stomach. In general, vagus section led to a doubling of the emptying time, without affecting the rate and frequency of peristalsis or the function of the pylorus. The alteration remained constant up to 4 months from the date of operation, without producing any effect on the general nutrition of the animals.

Bilateral resection of the coeliac plexus had no effect on the X-ray picture, either in size of stomach, rate of emptying, peristalsis, or pyloric function. The usual ulcers in stomach and duodenum were found after both types of nerve resection, duodenal ulcers being especially common after the sympathetic removal. The subcutaneous injection of morphia in doses sufficient to cause narcosis greatly increased the delay after vagus section, but had no appreciable effect on normal animals or on those in which the coeliac plexus had been removed.

In discussing the bearing of these experiments on the interpretation of the clinical picture of acute dilatation of the stomach in man, Nieden points out that the condition has most commonly followed operations on the upper abdomen in which drainage has been employed, and suggests that the sympathetic plexus is particularly liable to irritation under these conditions. He states that he has observed a case in which slowing of the pulse occurred before the symptoms of acute dilatation with increase of pulse-rate commenced, and interprets this preliminary slowing as evidence of vagus stimulation, followed later by vagus paralysis. He considers that morphia may be a contributory, but cannot be regarded as an exciting cause, and advises against its use when the condition is developed. He expresses no opinion other than a polite doubt as to the value of eserin or pituitrin, but thinks that the value of the standard treatment by posture may be connected with a slacking of the pull on the vagi at the cardia. More than half of the paper is devoted to a discussion of the various theories which have been put forward in explanation of the origin of acute dilatation in man. A list of more than forty cases published since 1911 is given, together with a bibliography of acute dilatation, of the results of vagus section, and of the

influence of drugs (morphia and inhalation anaesthetics) on the motor functions of the stomach.

This communication illustrates clearly the wide gap which at present separates the knowledge acquired by experimental work on animals from the clinical aspects of gastric and duodenal disease in man. From numerous reports on vagus section in dogs it is recognized that certain constant sequelae, viz. moderate chronic dilatation, delay in emptying, and the spontaneous appearance of ulcers, may be expected. The stomach, however, even when deprived of both vagi and of as much of its sympathetic supply as can be conveniently removed by operation, is still capable of carrying on its motor functions in an adequate fashion by means of its own intrinsic innervation. Until a method is found by which the latter can be attacked directly, speculation as to the nature of such a condition as acute dilatation can scarcely escape the reproach of being premature. E. K. M.

Giorgacopulo, D. Un caso di volvolo dello stomaco. [**A case of volvulus of the stomach.**] *Arch. Ital. di Chir.*, 1921, **4**, 660.

Nearly all cases hitherto described have had symptoms of acute obstruction from the outset, but this case, a man of 40, was seen in the stage of partial volvulus and diagnosed as stenosis of the pylorus. Three months before admission, when in good health, there was sudden onset, with vomiting, epigastric pain, and loss of appetite. The emesis became vehement and instant. Pain was very severe and only relieved when the stomach had completely emptied itself.

The upper part of the abdomen was distended and tender; no succussion; no free fluid in abdomen. Test meal gave free HCL 1·1 per cent.; no lactic acid; sarcinae and saccharomyces. Total acidity, 5 per cent.

There were traces of food in stomach 24 hours after ingestion. A pyloric carcinoma was suspected. At operation, on opening the abdomen, the stomach could not be seen, as the transverse colon lay between the liver and diaphragm. The pylorus was rotated through 180°. The greater curvature had turned upwards and forwards, so that the posterior surface was looking forwards; the fundus was not so fully rotated, but had moved in the same direction. There were no adhesions. There was no trace of ulcer or cicatrix, but the pylorus and muscular walls were much thickened; the stomach was dilated and in slight ptosis.

The stomach was easily restored to position, and—partly to deal with the pyloric stenosis, partly as a fixative measure—a retro-colic gastro-enterostomy was performed.

Recovery was uneventful, but a month later facial erysipelas occurred, and the patient died of pulmonary complications. The necropsy showed nothing further. There was a large vacant space between the liver and the sternum, and the gastro-colic omentum was short, but otherwise no abnormality was reported.

The author gives brief notes of eight of the fifty known cases. All save one were in adults, but Siegel has recently reported a gastric volvulus in a baby of two years. All agree in an anamnesis of considerable duration with 'gastric' symptoms, punctuated by attacks of greater or less severity at various intervals—with severe pain and vomiting, sometimes relieved by lavage, or merely by position—all terminating in an attack of the severity of acute obstruction. In several there was an actual hour-glass stomach,

and the torsion affected but one sac; in one the twist occurred in mid-stomach, so that only the pyloric portion revolved. The angle of torsion was often 360° or even more, and always in the same direction—the greater curve upwards and forwards. In one or two there was a defect in the gastro-hepatic omentum, and into it either colon, or colon and small intestine, or the pyloric sac, passed. In one the transverse colon maintained its normal position. In some gastroptosis or visceroptosis was marked, with relaxation of all ligaments.

Causation is purely conjectural, apart from the cases associated with diaphragmatic hernia and with gastric tumours. A case due to a fall has been noted, and some have been thought due to severe cough. The latter may be effective if the abdominal walls be very flaccid, the transverse colon full of gas, and attached to the greater curvature by a very short omentum.

E. R. C.

Razzaboni, G. La fisiopatologia del 'circolo vizioso acuto' consecutivo alla gastroenterostomia nei suoi rapporti colla occlusione alta. [**Physiopathology of 'vicious circle' after gastro-enterostomy and its relation to high obstruction.**] *Arch. Ital. di Chir.*, 1921, **4**, 553.

This article, with very copious bibliographies of its various sections, gives a useful *résumé* of the whole subject. In the first part there are studies of the 'vicious circle' from the aspects of operative technique, of the motor-function of the stomach after the various operations, of the clinical syndrome, and the pathogenesis. Notwithstanding all the possibilities of functional disturbance, whether neuro-reflex or chemico-reflex or toxic, and the great reduction of incidence rate with the perfection of technique, it is impossible to ignore the close resemblance of the condition to that of simple high obstruction.

In the second part, after a description of other experimental observations, the author narrates his own experiments on dogs, in two series. In the first the jejunum was divided six inches beyond its commencement, the distal end closed and the proximal inserted into the stomach at the usual site. In the second, after division at the duodeno-jejunal junction, the proximal end was similarly inserted. In both series there was, of course, complete virtual obstruction, and the result was invariably fatal after a few days, though with an interval of quiescence from persistent vomiting. The scanty urine (as in the two clinical cases recorded) contained albumin and sugar. The fluid of the vomit, or from the stomach or duodenum, proved to be extremely toxic when intravenously injected into rabbits. Many figures are given of the state of the intestinal and gastric mucosa, and of the liver, kidneys, suprarenals, and thyroid, all of which show evidence of toxic degeneration. The practical deductions amount to this: that the earliest possible opportunity should be taken for re-operation without wasting time on lavage or other measures, since the effect of the toxins found in the circle, however produced, act early and destructively upon all the glands of the body.

E. R. C.

Davis, Delmer L., and **Poynter, C. W. M.** **Congenital occlusions of the intestines.** *Surg. Gynec. & Obst.*, 1922, **34**, 35.

Davis having recently encountered a case of multiple atresia of the jejunum, the authors have searched the literature. They give a good

bibliography and specially quote papers by Theremin, Cordes, Kuliga, and Spriggs.

Imperforate anus is four times as frequent as intestinal atresias. Atresias are not constantly found at any particular part of the gut; they may be anywhere from duodenum to rectum; about 15 per cent. are multiple; occlusions of jejunum are about as common as those of ileum; this fact disturbs the theory that they are due to development errors of vitelline duct and ileo-caecal valve.

In Davis's case the contents of the blind sacs between the atresias were mucus, epithelial débris, many small round cells, and a few red blood cells. As in the cases of Kuliga and of Spriggs, the mucosa was degenerate, and the muscular coats atrophic. In the mesentery of Davis's case, where the gut was lacking, the arteries were sclerosed.

Various developmental errors have been suggested as aetiological factors, but there is no clear evidence; developmental accidents such as congenital volvulus (Gaertner) foetal intussusception (Braun, Chiari), foetal strangulation (Clogg), probably sometimes have an influence; foetal peritonitis was suggested by Fiedler as a cause; the authors, however, regard the arterial sclerosis, as seen in their case, as the primary lesion.

Treatment should consist in entero-anastomosis as soon as possible.

C. C. C.

Knight, H. O. An anomalous portal vein with its surgical dangers. *Ann. Surg.*, 1921, **74**, 697.

An abnormality found in a cadaver appeared so surgically important that it is described in full. The author has failed to find any note of a similar condition in surgical literature for the last five years, although the anomaly is well-known to anatomists.

The splenic vein arises from the spleen in the usual way, but on passing from left to right runs obliquely posterior to the middle of the body of the pancreas and emerges from beneath the body just below the neck of the organ. Immediately anterior to the head of the pancreas it is joined by two rather large veins coming upward in the root of the mesentery of the small intestine. These two veins, which represent the superior mesenteric vein, pass upward anterior to the horizontal portion of the duodenum. The junction of these two veins with the splenic vein represents the portal vein, which passes anterior to the upper flexure of the duodedum. At the upper border of the duodenum the vessel enters the right free margin of the gastro-hepatic omentum and in its course to the liver runs antero-lateral to the common bile-duct and hepatic artery. Therefore the vein lay in front of the duodenum, the common bile-duct, and the hepatic artery, so that in all operations upon the gall-bladder, common duct, or duodenum it would have been exposed to very serious danger.

The abnormality is due to a persistence of the left limb, instead of the right, of the caudal venous loop between the two vitelline veins.

A. J. W.

Graham, E. A., and Peterman, M. G. Further observations on the lymphatic origin of cholecystitis, choledochitis, and the associated pancreatitis. *Arch. Surg.*, 1922, Jan., 23.

Evidence is steadily accumulating that infections of the secreting glands rarely spread upwards along the ducts. In the present paper the

whole question of the nature of the spread of infection to the gall-bladder is discussed. The authors point out that there are four possible paths of infection: (1) descending by infection carried down in the bile; (2) ascending along the common duct; (3) haematogenous infections direct to the bladder and ducts; (4) spreading infection from an inflamed contiguous organ. They state that the first two theories only explain an infection of the mucosa and not the inflammatory changes in the walls, and this in spite of the fact that they have found that the changes in the deeper layers are usually more marked than those in the mucosa.

They produce evidence that cholecystitis rarely results from the entrance of bacteria into the gall-bladder. (1) They found that injection of organisms into a dog's gall-bladder did not cause definite cholecystitis unless the cystic duct or artery was ligatured. (2) In typhoid, bacteria are frequently found within the gall-bladder without cholecystitis.

They discuss the work of Koch and Rosenow suggesting a haematogenous path of infection. Mayer's work showed, however, that capillary embolism in typhoid was a rare occurrence, although he believed that infection could be carried in the bile and spread to the deeper layers from the mucosa. The association of cholecystitis with appendicitis and other inflammatory lesions within the abdomen is usually regarded as being due to a spread along the portal system to the liver and hence down the bile to the gall-bladder. Graham and Peterman believe that the evidence is so much opposed to such an infection from the bile that they cannot accept this explanation. Moreover, there cannot be a direct haematogenous connexion between the appendix and the gall-bladder unless the infection passes throughout the whole systemic circulation or there is a retrograde passage along the cystic vein. There is, however, through the lymphatics, a direct and simple route between the appendix and gall-bladder. They emphasize the close relationship to the lymphatics of the gall-bladder, the liver, and the pancreas. They have shown that in cases of cholecystitis, whether found in man or experimentally produced, hepatitis is constant, and that, if occurring secondarily to the cholecystitis, the right lobe is more affected than the left. Hence the infection must be by direct spread and not through the portal vein.

They have recently found that in a few cases of appendicitis the liver showed a hepatitis, and this suggested that the association of cholecystitis with appendicitis is due firstly to the hepatitis from which the infection spreads directly to the gall-bladder. They believe that the idea of a lymphatic origin secondary to a hepatitis explains the majority of cases of cholecystitis in man better than any other.

They bring forward evidence of a similar spread of infection from the gall-bladder to the pancreas, and they found that in seven dogs an injection of staphylococci into the portal vein was followed by a simultaneous hepatitis, cholecystitis, choledochitis, and pancreatitis. In six rabbits similar results followed after ligature of the cystic duct and artery, thus showing that the infection did not pass down the ducts. They sum up by saying that in many cases, probably the majority, cholecystitis represents a direct extension to the wall of the gall-bladder from a liver already inflamed. The infection is probably brought to the liver by the portal vein, or more rarely by the hepatic artery. Because of the intimate anastomosis between the lymphatics of the intrahepatic and extrahepatic systems there may be a direct extension into the gall-bladder as well as to the common duct and pancreas.

A. J. W.

Balfour, D. C. The technique of hepaticoduodenostomy, with some notes on reconstructive surgery of the biliary ducts. *Ann. of Surg.*, 1921, **73**, 343.

The difficulties which confront the surgeon when plastic or reconstructive surgery of the ducts becomes necessary are in marked contrast to the simplicity with which the common duct can usually be incised and explored. The most common conditions which give rise to the necessity of reconstructive surgery may be conveniently classified into two groups. The first includes neoplasms and fibrous strictures and the second injuries of the ducts during operation. The commonest cause of such an injury is the failure to recognize the cystic duct and the next common cause is that during an attempt to pick up a bleeding vessel the common or hepatic duct may be seized and crushed or even ligatured. Great stress is laid upon the importance of recognizing such an injury at the time, as repair is then much easier. It is when a reparative operation has to be undertaken at a later date that the difficulties are so great. Balfour describes in detail the method of direct anastomosis between the divided common hepatic duct and the duodenum, which was first reported by W. J. Mayo in 1905. A curved incision is made into the duodenum, which is then drawn up to the severed stump of the hepatic duct. The deep edges of the duodenal opening and of the hepatic duct are sutured together. The anterior flap of duodenum is then sutured over the hepatic duct and united to a capsule of the liver just above the hepatic duct. By this means a valvular opening is made. A. J. W.

Sauerbruch, F., u. Brunner, A. Die chirurgische Behandlung der Lungentuberkulose. [**The surgical treatment of pulmonary tuberculosis.**] *Ztschr. f. Tuberk.*, 1921, **34**, 335.

At the surgical department of the University Hospital in Munich, Sauerbruch and Brunner have operated on 57 cases of pulmonary tuberculosis between October 1918 and February 1921. In 43 cases, 11 ribs were resected; in the remainder, less extensive plastic operations were performed. The mortality within the first four weeks was 7 per cent., as compared with 12 per cent. in an earlier series of cases published by Sauerbruch. In the present series, 15 patients, i. e. 26 per cent., were freed of their sputum and tubercle bacilli by the operation, but, the observation period being short, permanent arrest of the disease is not claimed. In 42 per cent. improvement was effected, and in another 25 per cent. the patients were no better or worse. Apart from the reduced primary mortality, these results were much the same as those of Sauerbruch's earlier series of 381 cases with recovery in 35 per cent. and considerable improvement in 40 per cent. The admission is made that, though extra-pleural thoracoplastic operations can be carried out in different ways, they can never achieve the complete collapse of the lung seen in cases of total artificial pneumothorax. But experience has shown that by the paravertebral resection of the 1st to the 11th rib, and by the reduction of the volume of the chest by 300 to 500 c.cm., even severe cases may derive great benefit. With regard to the selection of suitable cases and the accurate estimation of the ability of the other lung to do the work of two, Sauerbruch and Brunner recommend a preliminary testing of the functional capacity of this lung by artificial paralysis of the diaphragm on the side most affected. The increased work thrown on the healthier lung by this device is often

sufficient to bring into prominence disease which is smouldering in the healthier lung. When activity of disease in the healthier lung is thus betrayed, and there is a rise of temperature or an increase of the physical signs in the healthier lung, the thoracoplastic operation is not undertaken. On the other hand, artificial paralysis of the diaphragm by a preliminary phrenicotomy may do much to reduce the sputum and temperature and encourage the operator to proceed with the more important step.

Sauerbruch and Brunner also point out that the operative treatment of cases of chronic pulmonary tuberculosis may do much to reduce the number of sources of infection. For though only about 10 per cent. of all cases of pulmonary tuberculosis are approximately unilateral, and about half of these are amenable to treatment by artificial pneumothorax, yet the remaining 5 per cent., which can undergo thoracoplasty, represent a very large number of cases, considering how many hundred thousand suffer in Germany alone from disease of the lungs. C. L.

Jacobaeus, H. C. The practical importance of thoracoscopy in surgery of the chest. *Surg. Gynec. & Obst.*, 1922, **34**, 289–96.

For ten years past Jacobaeus has been using the endoscope to study both the pleural and the peritoneal cavities, and has become enthusiastic as to the value of the thoracoscope for exploration and treatment.

The present paper concerns the performance of intrathoracic operations, such as division of adhesions with the cautery, under thoracoscopic vision. He has done this in 55 cases and other surgeons have used the method in about 30 more. Under local anaesthesia the thoracoscope is introduced through the back; the galvano-cautery is inserted through the antero-axillary line in the seventh, eighth, or ninth space; when the adhesions are high up near the apex he introduces the cautery 'still higher in the axillary line'.

Having found the cautery with his thoracoscope, not always an easy matter, he applies its platinum blade to the narrowest part of the adhesion and burns this through with the blade at dull red heat. Pain is usually moderate at this stage, but may be severe; thick firm adhesions may require considerable patience; the cautery must not be too bright or haemorrhage may ensue. He had one serious haemorrhage and another surgeon had a fatal case.

Post-operative complications include (1) a skin emphysema of no particular moment and (2) pleuritic exudates that may progress to empyema. In 50 cases Jacobaeus had 25 without exudate, 15 with slight exudate, 4 with pyrexia and persistent exudate, 4 with empyema, and 2 in which exudate only appeared one to three months after operation. Three of the four empyema cases eventually died. Gravesen and Holmboe have also found pleuritic exudates and empyemata the most serious complications.

In 35 out of 50 cases Jacobaeus had 'clinically successful results', Holmboe had 7 out of 12, and Gravesen 9 in 16.

The author has also found the thoracoscope useful in diagnosing tumours, afterwards operated upon by Key. C. C. C.

Holmboe, W. Et tilfælde av död efter adhærensavbrænding ad modum Jacobaeus. [**A fatality following cauterization of adhesions by Jacobaeus's method.**] *Norsk. Mag. f. Lægevidensk.*, 1922, **83**, 16–18.

Holmboe observes that in the first 100 cases of cauterization of pleural adhesions collected by Jacobaeus there was not one in which the cautery established a communication between the pleural cavity and a cavity in the lung. He records such a case. A few days after he had attempted, in a case of artificial pneumothorax, to divide a thick adhesion between the chest-wall and the upper part of the lung, a stinking pyo-pneumothorax developed which soon terminated fatally. He regrets ever having applied the cautery to such a solid adhesion, but he appears to regard this case only as a warning against cauterizing thick adhesions, not as indicating that this procedure is undesirable in carefully selected cases. C. L.

Platt, H. Pseudo-coxalgia (osteochondritis deformans juvenilis coxae: quiet hip disease). *Brit. J. Surg.*, 1922, **9**, 366.

This disease was first described by Hoffa in 1903 as a non-tuberculous arthritis comparable to osteoarthritis of later life, then by Legg and Calvé in 1909 and 1910, both these authors drawing attention to a peculiar flattening of the head of the femur and to a broadening of the neck. Perthes, in 1910 and 1913, also described the same disease. Many authors since the latter year have written about it, notably Legg in 1916 and Sundt in 1921.

Clinical picture. A disease of the first decade, it usually occurs between five and nine years, is more common in boys, and frequently presents a history of recent injury. Physical signs are often slight, with little or no atrophy of thigh and buttock, and no swelling of the soft tissue near the hip-joint. Limitation of movement is variable, between complete fixation due to muscular spasm in some cases and a more typical slight restriction of abduction and internal rotation in others. In both types the joint may be absolutely painless. After a variable period of active signs and symptoms, subjective phenomena gradually and completely subside, but some limitation of articular movement remains. The picture is thus one of a mild synovitis followed by osseous changes demonstrable in radiograms.

Writer's cases. 35 cases selected out of 300 cases of hip disease of various sorts. He divides them as follows:

Group 1.	Pseudo-coxalgia in childhood	18
„ 2.	End results in adult life	5
„ 3.	Arthritis deformans juvenilis of hip . .	5
„ 4.	Hip-joint affections with flattening of the head—coxa plana	7

Group 1. 18 cases—20 hip-joints. Unilateral 16, bilateral 2. Males 9, females 9. Right 12, left 8.

These are all cases showing the early changes of pseudo-coxalgia; radiograms of most of them are reproduced, in some cases further radiograms of the progress of the disease being added. The early radiograms mostly show flattening of the head and fragmentation of its bony nucleus, broadening of the neck, and sometimes acetabular changes.

Group 2. Adult cases. 3 males, 2 females.

These adults, except in one case, had had hip disease in childhood. The one exception is a man of 35 whose trouble began during war service.

Their radiograms all show enlargement of the head, which is too large for the acetabulum, and some show evidence of osteoarthritis.

Group 3. Arthritis deformans juvenilis coxae. 5 males, no females. Youngest 14, eldest 32.

All began between the ages of 14 and 17. Radiograms of these all show enlargement of the head and osteoarthritis. There is also acetabular change.

Group 4. Coxa plana. This group includes:

Chronic tuberculous osteomyelitis of the neck . . .	3
Tuberculous arthritis of the hip	2
Post-scarlatinal arthritis of the hip	1
Congenital dislocation of the hip	1

Radiograms of these all show flattening of the head.

Symptomatology and physical signs. Three stages with arbitrary limits are selected for description, namely, those of: 1. The onset. 2. The active stage. 3. The stage of recovery.

1. *Onset.* The symptoms are those of a mild synovitis of the hip and may be acute or insidious. Limping is present in all, but may be intermittent. Pain was present in half of the writer's cases, either in the hip alone or in both hip and knee. Slight irregular fever is common. Muscular spasm is present in most cases.

2. *The active stage.* This has somewhat vague limits and lasts from the appearance of the first subjective or objective phenomena to the stage at which the manifestations are so trivial as to give rise to the belief that recovery has taken place (*sic*). This stage lasts from about six to eighteen months. The limp, appearing at the onset, shows a steady tendency to disappear, returning from time to time. It is inconspicuous at all periods except during temporary existence of local pain and tenderness or of complete spasmodic fixation of the affected joint.

Spasm lasts only a very short time, leaving residual limitation of mobility. The spasm outlasts pain and tenderness. It fixes the hip sometimes in flexion and adduction, in contrast with the flexion and abduction of early tuberculous hip. Apart from the period of spasm, abduction and internal rotation are always, and flexion less commonly, limited. This restriction of movement is due to combined factors of localized spasm of the adductors, true shortening of the adductors, and the deformation of the femoral head causing mechanical changes in the joint. Perthes says that limitation of abduction persists in anaesthesia, but this is denied by Sundt.

The trochanter is prominent on the affected side. Very slight elevation is recorded by Legg and Perthes, but is difficult to measure. According to the writer, 'thickening in the trochanter is present in every stage of the life-history of a case of pseudo-coxalgia' (*sic*) and has a striking constancy as a sign. Palpability of the femoral head is emphasized by Calvé, but is not of importance according to the writer. The whole limb on the affected side is under-developed, but there is no localized wasting. Shortening is not present until there ensues a coxa vara deformity, which does not occur during childhood. Shortening from this cause may appear in later life. Apart from the X-ray findings the whole picture may be seen in certain types of coxa vara or in extra-articular tuberculous foci near the hip.

3. *Stage of recovery.* As the intensity of the subjective and objective signs diminish a stage of apparent recovery ensues, with preservation of

function of the hip-joint. When the limp has disappeared there remain trochanter thickening and limitation of abduction.

Radiographic manifestations. All hypotheses regarding aetiology have been founded primarily on the osseous changes seen in radiograms.

In most cases there is a definite cycle of osseous changes.

(A) *Changes in the head.* 1. Flattening. Early, with no enlargement in the lateral direction. No irregularity of ossification. 2. Further flattening with fragmentation. The bony nucleus breaks up into a number of pieces. Coincidently the head becomes expanded laterally, and creeps out in the direction of the trochanter. 3. Flattening with fusion of the fragmented pieces of nucleus, the head assuming a cap-like form. 4. The expanded flattened formation of the head persists throughout life.

(B) *Changes in the neck of the femur.* 1. Contour. The upper part broadens and the neck, as a whole, gradually shortens. No actual bending of the neck is seen, and the development of coxa vara emphasized by Calvé is apparent rather than real. 2. Internal structure. An ill-defined zone of alteration in calcification produces a spongy area in the upper part of the neck. A more regular arrangement of areas of condensation and rarefaction is sometimes seen, associated with marked fragmentation and flattening of the head.

(C) *Changes in the acetabulum.* These, by most writers considered as inconspicuous, consist in the adaptation of the cavity to the altered shape of the head. Where destructive signs are unusually well marked in the femoral head, acetabular changes are equally striking.

French writers have described a widening of the space between the head and acetabulum. This is present in many radiograms but its significance is obscure.

Chronology of changes in head, neck, and acetabulum. All advance and recede together. There is no justification at present for allocating a primary position to the change in either the head or the neck.

Relation of radiographic changes to clinical findings. Abnormal radiographic changes must have been present in many cases for a considerable period before the onset of symptoms. Changes demonstrable radiographically, become well established during a silent clinical stage, progress still further during the period of appreciable symptoms and manifest objective signs, and continue to advance long after their subsidence. The clinical stage of spasm does not correspond with any one of the radiographic pictures and may occur early or late in the course of the disease, as shown by X-rays.

Clinical and radiographic end results. The acquisition of a permanently deformed head is the rule.

The later results in adult life are suggested by the radiograms reproduced of the writer's group 2, which subdivide themselves into two sub-groups:

(*a*) Cases with symptoms of chronic joint strain.

(*b*) Cases with chronic arthritis.

Other authors have described end results both of arthritis deformans and of essential coxa vara. The author considers that these are to be considered as disabilities of the hip-joint superadded to the pre-existing deformed head of pseudo-coxalgia.

Aetiology and pathogenesis. *Frequency*: Figures vary from 41 cases of pseudo-coxalgia out of 243 alleged tuberculous hips to 4 cases in 1,000 hips examined for miscellaneous conditions. *Sex*: Commoner in boys. *Heredity*: No evidence of any hereditary influence. *Age*: Second half of

the first decade; in contradistinction from tuberculosis, which affects typically the first half.

Bilateral affection is rare.

Theories of pathogenesis fall into two groups. The first school considers that the disease is a definite pathological entity with a specific cause; the second, that it is a morbid anatomical change possibly due to a variety of causes acting singly or in combination. The author then discusses these possible pathological factors. Although Legg and others held trauma as the sole determining cause, the author dismisses the aetiological influence of injury, rickets, congenital anomalies of ossification, and syphilis; he believes that the essential cause of pseudo-coxalgia, and also of Schlatter's disease and of Kohler's disease of the tarsal scaphoid, is infection with pyogenic organisms of attenuated virulence. He also suggests that the response of the hip to such low-grade infection is, in the first decade, pseudo-coxalgia and, in later childhood, arthritis deformans juvenilis, the alteration of type being due to the changes in vascular supply of the hip occurring at adolescence.

Treatment. The disease has a tendency to spontaneous recovery. Immobilization from an early period may retard but does not avert the cycle of bony changes. There is no evidence to show that treatment can influence the cycle of bony changes when these have become well advanced.

Operative exploration of the hip-joint is of pathological interest but is not an established curative measure. J. T.

McCarrison, R. Fats in relation to the genesis of goitre. *Brit. M. J.*, 1922, i, 178.

Continuing his researches on the effects of abnormal diets upon disease, McCarrison has carried out a series of experiments to determine the effects of the administration of fats upon the thyroid gland. The experiment was carried out in the Nilgiri Hills of Madras, where goitre is practically unknown.

Series of pigeons were taken and confined in cages. One series was fed on a mixture of 28 ounces of mixed seeds with 3 ounces of butter. The next series had a similar diet, but to the mixture was added 6½ ounces of freshly-chopped onions. The third series received a mixture of seeds only and acted as controls.

These experiments showed that there was a very considerable increase in the weight of the thyroid in those birds which received the addition of butter. In fact the average weight of the thyroid gland was over twice that of one of the controls. When the chopped onions were added the average weight was 1·5 times that of a control. Microscopical examination showed that the thyroid of the birds receiving the butter had little or no colloid and a considerable overgrowth of the epithelium. The administration of chopped onions resulted in a very distinct protective impulse and tended to reduce the average size of the thyroid enlargement.

McCarrison lays stress, however, upon the fact that 35 per cent. of those that received butter showed no abnormality of the thyroid, suggesting that the excess of fat was not the cause of a goitre but was only a contributing factor. He suggests that it makes the gland more prone to the action of bacteria. Although there was a distinct increase in the epithelium of the gland there was no clinical evidence of Graves's disease.

A second series of experiments was performed. The control birds

were given a mixed grain, others in addition were given butter, cod-liver oil, or oleic acid. In this experiment it was found that the incidence of goitre was as high in the controls as in the birds that received butter or oleic acid, but it was not present in those which received the cod-liver oil. The thyroid was, however, bigger in the birds which received butter and oleic acid.

He concludes from this that close confinement, want of exercise, overfeeding, and contamination of the food are potent factors in the cause of goitre. Cod-liver oil affords a complete protection against these factors. The butter and oleic acid favoured the development of the thyroid enlargement. He regards the protection of the cod-liver oil as due to its high percentage of iodine.

Experiments were then carried out on tadpoles. These tadpoles were fed on flour-caseinogen. To the food of other groups were added butter, oleic acid, or cod-liver oil. In yet others small doses of iodine were added. These experiments showed that an excess of fat caused a remarkable retardation in the rate of growth. Iodine prevented the retardation caused by butter and oleic acid, but increased that caused by the cod-liver oil. The rate of metamorphosis was delayed in a similar manner. The retardation of growth was associated with delayed development of the thyroid, which was also compensated for by iodine, excepting in the cases caused by the cod-liver oil. A. J. W.

Marion, G. La pyélotomie élargie. [**Extended pyelotomy.**] *J. d'urol. méd. et chir.*, 1922, **13**, 1.

By this procedure Marion avoids the performance of nephrolithotomy in cases of calculi not exclusively contained in the renal pelvis. Branched calculi up to 8 cm. in height have been removed by it. The operation consists in prolonging the ordinary oblique incision in the renal pelvis into the renal parenchyma in the direction of the calculus, using the radiogram and direct contact of the calculus as guides. It may be necessary to prolong the incision in two directions, making a Y-shaped incision. In making the incision the retro-pelvic branch of the renal artery is necessarily divided, but the haemorrhage is not comparable to that produced by incising the external border of the kidney: the two ends of the artery are ligatured after removal of the calculi. Following the operation, no more blood appears in the urine than after an ordinary pyelotomy. The operation is indicated in calculi which extend from the pelvis into the kidney in one direction only and in coral calculi which only extend a short way into the kidney; it is contra-indicated in the ordinary form of coral calculi, in calculi exclusively in the kidney, and in multiple calculi scattered throughout the kidney.

F. J. F. B.

Usland, O. Appendicit og urinveisinfektion. [**Appendicitis and infection of the urinary system.**] *Med. Rev.*, 1922, **39**, 3.

Among 34 cases operated on for acute appendicitis between October 1920 and May 1921, Usland has found 20 in which the urine showed pathological changes; in the remaining 14 it proved sterile both on direct and cultural examination. In 10 of the cases with infected urines frequent bacteriological examinations were made, the urine being obtained by catheterization under aseptic conditions. In 10 cases of acute appendicitis with infected catheter urine and under close (bacteriological) observation

both before and after operation, the following microbes were found in the urine: Staphylococci plus *B. coli* in 4 cases, streptococci plus *B. coli* in 1 case, staphylococci alone in 4 cases, and *B. coli* alone in 1 case. All the 16 cases of infected catheter urine showed sterile urine on discharge from hospital after appendectomy.

A comparison of the appendix findings in the two groups of cases showed no uniform differences, with this exception: retention of inflammatory products in the appendix was commonly associated with infected urine. Thus, in 13 cases of appendicitis with infected urine there were definite signs of retention in the appendix, whereas the 14 patients with normal urines usually suffered from slight catarrhal appendicitis or limited gangrene with early perforation. In the 10 cases referred to, the urine was examined every other day after the operation, and in every case it became sterile in from 10 days to 3 months, the time taken in most cases for the urine to become sterile being 10 to 14 days. In 4 cases catheterization of the ureters and cystoscopic examination of the bladder were undertaken after the operation; in 3 cases both kidneys proved to be infected, and in 1 infection was limited to the right side. Usland records in detail 5 cases, showing how the symptoms of disease of the urinary tract may dominate the clinical picture, while the symptoms of appendicitis may be comparatively slight and indefinite. In 3 of these cases the patients had been under treatment for disease of the kidneys or bladder before they came to operation for appendicitis, and in every case urine from the right kidney showed morbid changes while urine from the left kidney was normal. In some of these cases the urinary symptoms had lasted for several years, and treatment with salol and urotropine or with silver nitrate irrigations had proved futile. In all these cases removal of the diseased appendix banished all the symptoms from the urinary system, and the urine became sterile in 10 to 60 days. In every case a scrutiny of the mouth, throat, tonsils, nose, nasal cavities, and middle ear was undertaken with negative results. Usland concludes that in these 5 cases the primary focus of infection was the appendix, and that they give force to the teachings of Billings and Rosenow as to the importance of focal infections. C. L.

Josefson, A. Indblåsningar av gas i kroppens halor och organ i diagnostiskt syfte. [**Diagnostic injections of gas into the cavities and organs of the body.**] [**B.**] *Hygeia*, 1922, **84**, 1.

Josefson's review of the literature of diagnostic gas injections shows that there is hardly a cavity or organ in the body into the privacy of which gas-injecting enthusiasts have not intruded. His paper deals chiefly with diagnostic injections of gas into the spinal canal and the peritoneal cavity; with the importance of the former he is greatly impressed, whereas he has little good to say of the diagnostic pneumo-peritoneum. In more than 10 cases he has replaced cerebrospinal fluid by air, and in 3 the X-rays showed the exact level at which the further ascent of air in the spinal canal had been arrested by morbid processes. Considering how difficult it is in many cases to determine the level at which a tumour of the cord occurs, this aid to locating a tumour is invaluable. In several cases injection of air into the spinal canal caused discomfort, particularly when the patient was made to sit up, or showed an unexpected obstruction above the level of the injection, but no permanent ill effects were noted. Josefson describes as a new sign

of obstruction within the spinal canal the following observation : When this canal is obstructed above the site of injection, gas soon reappears in the tube through which it has been injected, and sometimes liquid ceases to escape, the spinal canal below the obstruction being evidently filled by gas alone. In one such case an operation showed that above the tumour there was cerebrospinal fluid, while the injected gas was below it. Conversely, if cerebrospinal fluid is obtained at every injection of gas, there is probably free communication throughout the spinal canal. Josefson also discusses appreciatively the work of Dandy and others on the diagnostic injection of gas into the ventricles of the brain (*Annals of Surgery*, 1918 and 1919).

Josefson's discussion of diagnostic pneumo-peritoneum resolves itself into a piling up of all the accidents that may happen or actually have happened. These include troublesome surgical emphysema, peritonitis, great general discomfort, injury to the intestine, puncture of important veins with subsequent gas embolism, and sudden heart failure. The advantages which might compensate for these drawbacks are minimal, and an analysis of 16 cases of diagnostic pneumo-peritoneum induced since 1920 by Josefson has convinced him that in none did the patient derive real benefit, and in none did this procedure lead to radical change of treatment. He refers to two fatalities published in 1921 in the *Berliner klinische Wochenschrift*, death in one case being due to air embolism. As a competitor against simple exploratory laparotomy, diagnostic pneumo-peritoneum deserves little praise.

C. L.

Jacobæus, H. C. On insufflation of air into the spinal canal for diagnostic purpose in cases of tumours in the spinal cord. *Acta Med. Scand.*, 1921, **55**, 555.

Since 1909 Jacobæus has been investigating the therapeutic and diagnostic effects of injecting air into the spinal canal. The therapeutic results of replacing the cerebrospinal fluid by air in cases of tuberculous meningitis were disappointing. But in several cases of tumour of the cord he was able to locate with fair accuracy the level at which the tumour occurred by noting by X-ray examination the height to which the air ascended in the spinal canal. In two cases the upper limit of the column of air corresponded well with the lower limit of the tumour as found at a subsequent operation. In a third case the upper limit of the air was somewhat below the lower limit of the tumour; it was not clear whether the air did not travel higher because of adhesions or because too little had been injected. Jacobæus concludes that within that part of the spinal canal where the air column clearly appears, there can hardly be any tumour. He notes with surprise that Wideröe, of Christiania, was unable by X-ray examination to see any column of air in the spinal canals of the 11 cases given intraspinal injections of air. C. L.

Gobbi, L. Contributo allo studio dei tumori endoteliali. [**Contribution to the study of endothelial tumours.**] *Policlin.*, 1922, **29**, Sez. Chir., 23.

The basis of this review of the vexed question of the endothelioma as a pathological entity and its exact position in relation to the carcinomata and sarcomata, is a case of tumour of the corpora cavernosa in a baby of ten months.

The general structure was very definitely perivascular; the haemic vessels or 'sinuses' retained their endothelial lining perfectly normal and intact, and the contents were normal blood cells. The connective tissue of the walls was definite and complete, if perhaps a little abnormally thick, and the cells of the tumour were in direct contact with it, lying radially and of fusiform to cylindrical shape in their innermost row. As the cells—though preserving their general arrangement around the vessel—were followed farther and farther away they lost their fusiform character and became polyhedral to round. Their protoplasm was clear or finely granular; the nuclei generally single and round, large, and darkly staining, but occasionally multiple, with active but irregular kariokynesis and chromotaxis. There was a definite intercellular substance finely fibrillar and retiform. There was no trace of proliferation of lining cells of perivascular lymphatic spaces, and the appearances strongly suggested a connective-tissue derivation.

Some ten cases of sarcoma of the corpora cavernosa or the corpus spongiosum are abstracted from the literature, of which six have close relations to the one figured and all are classed as endotheliomata. All occurred in adults. The author, admitting that it is a moot point whether there be, in the vessels and vascular spaces of spongy tissue, any true 'perithelium' in the sense of Eberth's description of it for vessels of the pia, nevertheless justifies the use of the description 'perithelioma', in this instance at least, from the very intimate relation of the cylinders of cells to a central vessel, normal on the luminal aspect, and suggests that the histological features ally it and endotheliomata to the sarcomata rather than carcinomata. E. R. C.

Romiti, C. Parotite cronica policistica. [**Chronic polycystic parotitis.**] *Policlin.*, 1922, **29**, Sez. Chir., 45.

Study of other reported cases, of experiments on ligation of the parotid duct or on the effects of partial separation of parenchyma from the duct, together with histological examination of his own case—which occurred in an accessory lobe or gland—leads the author to the conclusion that whilst some cases may arise from embryonal, undifferentiated rests, some from foetal or differentiated inclusions, and others from bronchial elements, there is a class of cases in which a cyst or cysts of considerable size may be the outstanding clinical feature, but in which examination of the whole gland or lobe reveals few or many smaller cysts in all stages of formation, together with widespread changes in the connective tissue. These changes, which consist in marked interacinous and pericanalicular proliferation, are responsible—as the new young fibrous tissue-cells pass through their phase of contraction—for a gradually increasing difficulty in the escape of secretion by the ducts, and are accompanied in their early stages by a steady proliferation of the parenchymatous elements. Atrophy only results in the late stages when, the smallest ducts and their acini having become dilated, the increasing obstruction to outflow becomes absolute. Then the atrophy may result in the disappearance of the tissue between adjacent cysts and the formation of larger and larger cysts which often are saccular or show evidence of bridles or partial septa in their interior. In these cases the contents of the cyst may show chemical evidence of their salivary origin.

The author suggests affinities between the cysts thus produced and those found in some forms of polycystic mammae and in some of cystic

degeneration of the kidneys. Notwithstanding the title chosen for his paper, the question of the source of the 'Parotitis' and of its partial distribution is not discussed. E. R. C.

De Quervain, F. A consideration of the relative merits of resection and gastro-enterostomy in the treatment of gastric and duodenal ulcer. *Surg. Gynec. & Obst.*, 1922, **34**, 1–4.

A short account of the operative results of 247 cases of ulcer treated at De Quervain's clinic at Berne between 1910 and 1921. As regards special methods of diagnosis, the experience was that little value is to be attached to the hydrochloric acid content of the stomach. Exact localization by X-ray was possible in 87 per cent. of gastric and in 54 per cent. of duodenal ulcers. The operative mortality was 6·5 per cent. for gastro-enterostomy and 7·7 per cent. for resection, the former operation being reserved for cases in poor condition. In three-fourths of the post-operative fatalities lung complications were the cause of death, and were dependent on the extent of the operation rather than on the kind—local or inhalation—of anaesthetic employed.

The author attributes jejunal ulcer mainly to the use of non-absorbable suture material and to pyloric exclusion. The cases were followed up and gastro-enterostomy was found to have given good end results (i. e. four years after operation) in 75 per cent., resection in 80 per cent., or, if V-shaped excision be excluded, in 90 per cent. In duodenal ulcer, gastro-enterostomy gave 65 per cent. of cures, the number of resections being too small to allow of comparison. De Quervain considers that, provided the operative risk be good, the interests of the patient are best served by resection in both gastric and duodenal ulcer. E. K. M.

Mau, C. Die Magen-Colonresektion bei Carcinoma Ventriculi. [**Resection of colon in carcinoma of the stomach.**] *Deutsche Ztschr. f. Chir.*, 1921, **165**, 216–56.

Mau records 18 cases in which resection of part of the colon was performed in combination with the removal of a malignant tumour of the stomach. The cases were spread over the period 1910–20. He gives a full discussion of the technique, with special reference to the value of one-stage and two-stage operations. He considers those cases inoperable where the primary growth, in addition to attachments to the transverse colon or meso-colon, is also adherent to pancreas, liver, or spleen.

The necessity for colon resection arises on account of the great liability of that part of the bowel to necrosis after ligature of its vessels. Ligature of the trunk of the middle colic artery is invariably followed by necrosis, which usually extends from hepatic to splenic flexures. Ligature of even a small branch of the artery, if followed by the slightest discoloration of the colon, is liable to lead to necrosis up to fourteen days after operation. Mau insists that, where removal of the stomach has necessitated any interference with the blood-supply of the colon, the viability of the latter should be tested by seeing pulsation in the smallest visible arteries of the bowel-wall or by seeing blood spout from the stump of an amputated appendix epiploica. After a discussion of whether the resection of stomach and colon should be carried out in one mass or at separate operations two days

apart, he urges the former because estimation of the viability of the colon is uncertain, there is less risk of cancer dissemination, and the removal of lymph glands is more thorough.

There is, at present, division of opinion as to whether the ends of the colon should be brought out to the surface or the continuity of the gut restored immediately. In the collected cases the mortality of the two types of operation has been identical, i.e. 55 per cent. There is therefore no advantage to be gained by the two-stage operation, except in the case of patients who are in such poor condition that the saving of the additional time is of paramount importance. Except in the strictly limited number of cases where the damaged segment of colon is so short that end-to-end union can be performed, Mau advises ileo-sigmoid anastomosis and removal of the large bowel to a point as near the splenic flexure as can conveniently be reached. Closure of the ends with caeco-sigmoid anastomosis has frequently led to accumulation of contents in the occluded ascending colon and perforation or giving way of the suture line.

From the clinical side he points out that 4 of his 18 patients gave a history of less than 14 days, and that in every case the necessity for colon resection only appeared on opening the abdomen. Two out of 18 cases have lived for over three years.

[NOTE.—This paper is of value chiefly in so far as it indicates the recorded results of the various technical procedures in an operation which is, to judge from the literature, but seldom carried out by the majority of surgeons. It is unusual to find references to the difficulties introduced by adhesions to the colon or mesocolon, and it is probably fair to assume that the common practice in most countries is to separate such adhesions where possible and to regard as inoperable cases which would need the extensive manipulations which the author discusses. Mau does not disregard this point of view, but urges that, since of his 17 patients who died of recurrence 11 lived for more than 12 months, while the average duration of life of patients with a palliative gastro-enterostomy is 6 months, the advantages of the more severe operation, considered as a palliative only, outweigh its high initial mortality.] E. K. M.

KURTZAHN. Verfahren zur Erzielung der Kontinenz bei Anus praeternaturalis. [**A method for securing control of artificial anus.**] *Deutsche Ztschr. f. Chir.*, 1921, **167**, 129–38.

The operation suggested by the author is an adaptation of the skin-lined tube which has become familiar in connexion with the kineplastic surgery of amputation stumps. The method employed for the formation of a controlled iliac anus after excision of the rectum is to bring the proximal end of the colon out through a stab in the abdominal wall roll up a square of skin into a tube running at right angles to the long axis of the bowel, lay the latter across the superficial aspect of the skin tube, and then cover it with a second flap of skin. When the operation is completed the colon can be compressed between a rod in the skin tunnel and a pad on the surface.

Two cases are quoted, in which continence was successfully maintained. In the first a temporary faecal fistula followed compression applied over a metal rod in the skin tube, and Kurtzahn therefore advises the use of a solid rubber cord, the ends of which are attached to the truss carrying

the compressing pad. The method can also be used for a colostomy in which both ends are brought out, the proximal colon only being controlled by skin tube and covering. The illustrations attached to the article are self-explanatory. E. K. M.

NEUROLOGY

Rivers, W. H. R. ***Instinct and the Unconscious. A contribution to a biological theory of the psycho-neuroses.*** Cambridge University Press, 2nd edition, 1922.

That a second edition of Dr. Rivers's book has been so soon called for indicates the widespread interest aroused by its subject-matter. The very favourable reviews by which it was greeted on its first appearance foreshadowed this success, and indeed, when we recall the author's many qualifications to speak with authority on the subject of the psychoneuroses it must be conceded that his opinions demand the most respectful consideration. Not only does he bring the fruits of his own studies on the psychology of the special senses, and those of his collaboration with Dr. Head on the physiology of the sensory nervous system to bear upon the problem, but he is one of our greatest authorities on the psychology of primitive peoples, and during the late war he may be said to have rounded off this wide and varied experience by direct clinical contact with the neuroses of war. It was to be anticipated, therefore, that he would approach the problems presented by the psychoneuroses from a new and interesting point of view. As far as we can recall, however, those who reviewed the first edition of the present book were psychologists exclusively preoccupied with their own subject, and apparently willing to accept without comment that deeper-lying aspect of Rivers's hypothesis which is implied in his sub-title. Since the hypothesis must stand or fall with its biological foundation, the omission to consider the latter is the more remarkable. In the circumstances, a brief discussion of this side of Rivers's book may be not without interest. As we understand the author's argument it is that in the processes of inhibition on the physiological levels of the nervous system he finds an analogy to, and an explanation of, that process of suppression on the psychological level by which unpleasant experience is banished to the unconscious. Following the conception we owe to Head and his collaborators, Rivers believes that on the physiological levels of the nervous system there are certain primitive forms of sensory and motor activity which have been uninterruptedly inhibited or suppressed from an early stage of the phylogenetic history of the race, but which, under the conditions of disease or injury of the nervous system, may be released from suppression and suddenly reveal their continued existence in an outburst of unimpaired activity.

Similarly on the psychological level instinctive processes long since buried beneath more recently developed and more discriminative mental activities, but by no means abolished, may suddenly show themselves in the disorders of a psychoneurosis. In the light, therefore, of certain supposed physiological examples of inhibition and subsequent release of function in the nervous system, Rivers sets out to formulate a biological and evolu-

tionary theory of the instinctive reactions and of the psychoneuroses, and to draw attention to certain features of close resemblance between physiological and psychological processes.

Our knowledge of the evolution of form and structure rests upon a sure foundation of observation, and the process of recapitulation during foetal development is one of the most striking proofs of this evolution. The problems of the evolution of function, on the other hand, are much more complex and obscure. In its biochemical aspects, certainly, function does not seem to have altered in the course of evolution. The adrenalin of the human subject is identical in constitution and function with that in the most primitive animals in which it is to be found. Similarly, in the physico-chemical processes which lie at the root of all nervous activity, there has probably been little modification in the phylogenetic history of the race. Even in the case of the nervous processes concerned in the co-ordination of movement, to take one of the best understood examples of nervous activity, the fundamental characters of reflex reaction and of co-ordination of reflex are the same over a very wide range of the animal kingdom. The simple reflex reaction in the coelenterate and the simple reflex in the mammal differ in no essential respects. However, on the higher levels of the nervous system an inconceivably complex elaboration of function has occurred, but even here the processes underlying these numerous and highly refined functions are the same as those which obtain on the lower reflex levels of the nervous system.

Now, Rivers's theory implies the possibility of a process of permanent inhibition, and it assumes that a function can lie extinguished, as it were, under the influence of such an age-long inhibition, and yet spring into unimpaired activity immediately upon the removal of this suppression. It also assumes that the particular neurological symptom-complexes which he has chosen as his examples of such release of primitive function can with certainty be identified with the hypothetical primitive nervous activities he postulates.

On both these fundamentally important points we believe that Rivers has failed to establish his case. In the whole range of physiological knowledge we can find no evidence of a process of permanent inhibition, nor any support for the view that a function can suffer an indefinitely prolonged suppression, in this case throughout the greater part of evolutionary history, with the complete immunity implied in Rivers's hypothesis. On the clinical side, also, we believe that his interpretation of the particular symptom-complexes he has chosen as his examples is not in accord with such knowledge as we have obtained from the physiological analysis of symptoms in disease and injury of the nervous system.

We may now pass on to consider these examples in detail. They are chosen from the work of Head and his collaborators, and although Rivers has himself been among the most distinguished of these collaborators, yet we find more than one serious divergence in the present exposition of this work from that to be found in the original papers. The first of these physiological examples is taken from the observations of Head and Rivers upon the disorders of sensibility resulting from section of a peripheral nerve. Their experiment in human nerve division led them to the view that there are two anatomically and physiologically distinct mechanisms in the cutaneous nerve-supply. One, the more primitive, they called the protopathic system. This is subserved by nerve-fibres

of its own, and, except in the case of tactile sensibility, has its own nerve-endings in the skin. In virtue of this system the subject is capable of appreciating extremes of temperature, pain, and a crude form of touch. The qualities of these modes of sensibility are very peculiar. In Rivers's words they 'just enable one to know that something is there and that it is pleasant or unpleasant', and there is 'no power of distinguishing differences in intensity nor of telling with exactness the spot stimulated'. This form of sensibility 'is consistent with its being the representative of the sensibility of an animal which possesses only the power of becoming aware of changes of a crude kind and, according as these changes are pleasant or unpleasant, of reacting at once by such mass movements as would take it nearer to, or remove it from, the source of stimulation'. There is 'no necessity for the discrimination which would enable the exact perception of the nature of the object'. Finally, 'these features would furnish elements of vagueness and confusion wholly incompatible with the exact power of localization which developed later and enabled the animal to modify its behaviour to the nature of the external object by which the sensations were being produced.' Under normal conditions this primitive sensory system is supplemented by a more highly developed mechanism, also endowed with its own peripheral nerves and endings, though there are no details given as to the nature of the latter, except in the case of touch, where the system shares the touch spots of the protopathic system. This epicritic system is of much later development and its functions are not alone to add fresh qualities to cutaneous sensibility, but also to provide a discriminating and graduating element and to inhibit those components of the protopathic system which would be detrimental to the organism in its more highly evolved forms. Here, then, we have a primitive mechanism permanently held in check by a more highly specialized one, and its existence never suspected until revealed by the experiment in question.

The second example is taken from Head and Riddoch's observations upon the 'mass reflex' of spinal man. This group of conflicting and violent reaction they, and Rivers following them, interpret as the expression of a primitive mechanism released from an age-long suppression by removal of higher nervous control.

In an earlier review in this journal (*Medical Science*, 1921, **4**, 141) on the elementary nervous system, we pointed out that there is absolutely no evidence that 'crude' nervous mechanisms such as are postulated in these theories have ever existed. On the contrary, from its earliest appearance the nervous system, as studied by Parker and others in such primitive animal forms as the coelenterata, has been capable of achieving exact localization of peripheral stimuli and of graduated and minutely discriminative responses. In such animals the nervous system may be extremely simple, but within its small range of activity it is always found to be an instrument of precision. Moreover, in respect of Head and Rivers's theory of the constitution of the peripheral sensory nervous system, there is a weighty mass of observation and opinion directly conflicting both with the facts of observation recorded by Head and Rivers and with their conclusions (cf. Trotter and Davies, *J. Physiol.*, 1909, **38**, 134, and *J. f. Psychol. u. Neurol.*, 1913, **20**, Ergänzungsheft, 102). In respect of the 'mass reflex' there are also grounds upon which, at the very least, we are justified in regarding the original interpretation as unproven (cf. *Brit. M. J.*, 1921, ii, 837, and *Medical Science*, 1921, **4**, 427).

Rivers's third example of inhibition on the physiological level is taken from the thalamic syndrome. In lesions of the thalamus a characteristic symptom-complex is sometimes observed. Not only is there impairment of certain aspects of sensibility, but in addition there may be spontaneous pain and a peculiar over-reaction to the affective side of sensation and to emotional states. According to Head, the thalamus is a primitive sensory organ primarily concerned with the affective aspect of sensation. Normally it is under the control of the more recently and more highly developed sensory cerebral cortex, which for countless ages has inhibited certain features of thalamic activity. Lesions cutting the thalamus off from cortical influence release the former, and its primitive activities—though possibly modified in the course of evolution—reappear with all their old vigour. Rivers defines the thalamus as 'the central representative of the protopathic aspect of sensibility', and suggests that typical protopathic sensibility does not appear as part of the thalamic syndrome, because the suppression of protopathic characters 'is still being maintained at the periphery'. There are many reasons for regarding this interpretation of the syndrome as being no less speculative than those we have already discussed in connexion with Rivers's previous examples. In the first place, the thalamic over-reaction appears not to be a constant component of the syndrome, as a case recorded in the present number of *Medical Science* illustrates. Secondly, the anatomical disposition of the fibres joining cortex and thalamus is such that it is hardly possible for cortico-thalamic fibres to be interrupted without simultaneous interruption of thalamo-cortical fibres. In other words, cortical control could hardly be removed without equally complete loss of the cortical aspects of sensibility. Yet several of Head's case records show that the disturbance of the latter was minimal, while the intensity of the thalamic reaction bore no relation to the degree of impairment of the cortical aspects of sensibility. Moreover, interruption of cortico-thalamic fibres never results in thalamic overaction unless the thalamus itself is actually involved in the lesion, whereas interruption at any point should be adequate to produce this result. In these circumstances, the probability of thalamic release and overaction seems scarcely to enter into the question, and an explanation more capable of comprehending the facts of observation must be sought. It is here particularly that Rivers seems most clearly to depart from the views of Head, and indeed from a very important physiological law of nervous activity. We believe that Head does not allow the employment of the term 'protopathic' in connexion with the central nervous mechanisms of sensation, while he clearly states his belief that inhibition of the protopathic elements of cutaneous sensibility takes place at some higher level than that of the termination of the fillet in the thalamus. So that Rivers's statement that it occurs largely at the periphery not only departs from that of Head in this important respect, but it seems to imply, what we know not to be the case, that inhibition is a function of the peripheral nervous system. In the higher animals peripheral inhibition does not occur, except in connexion with the involuntary nervous system.

We are therefore compelled to conclude that Rivers's examples of inhibition on the physiological level have been unfortunately chosen and do not support his biological theory, which, it follows, remains unproven.

When he comes to deal with the *instinctive reactions*, we find Rivers equally difficult to follow. He quotes and attempts to apply both to so-called 'protopathic' motor and sensory reactions and to instinctive reactions

the 'all-or-none' principle of conduction of the nerve impulse. This relates to a physico-chemical process in the nerve-fibre, and the work of Keith, Lucas, and Adrian in this connexion is referred to by Rivers. We believe that this principle cannot be validly applied to the physiological reactions described by Rivers, while in the case of psychological processes any value it might have is neutralized by the numerous exceptions and qualifications which he finds it necessary to make. For example, in a comparison between the characters of instinctive behaviour and so-called protopathic sensibility, Rivers regards both as the product of subcortical activity and as sharing the thalamus as their central organ. Instinctive reactions are immediate and unreflecting, they are maximal and unvarying. In other words, they show an 'all-or-none' character. But here, as on its purely physiological side, the theory involves the most far-reaching assumptions. Thus, we are told that the instinctive reactions of insects, which we know to be graded and discriminative, were originally 'crude modes of response', and that they have been regulated and modified by some hypothetical process of control which is said to be quite different from that adopted in the case of the vertebrate nervous system. Hence we have 'epicritic' and 'protopathic' instincts, the latter becoming epicritic under the influence of suggestion and intuition. In his conception of instinctive *reactions to danger*, Rivers invokes physiological principles still further. He gives five such reactions, namely, flight, aggression, manipulative activity, immobility, and collapse. Flight and aggression are simply protopathic 'all-or-none' reactions containing no trace of inhibition or suppression. Immobility, on the other hand, he regards as fundamentally different from these. It consists in the suppression of movement, in inaction, and is associated with the suppression of pain and fear. It is perhaps the earliest appearance of suppression as a controlling mechanism. We believe this view to be untenable. *Immobility is reaction by posture*, just as flight is reaction by movement. The maintenance of posture is as positive and as active a reaction as flight, and in both inhibition plays an integral and an identical part, as the researches of Sherrington have amply shown. Further, to suppose that the immobile animal is actively suppressing the impulse to fly and is inhibiting fear and pain is a purely anthropomorphic speculation. In this connexion some observations recorded by Golla in his Croonian lectures (*Medical Science*, 1922, **6**, 41) are of considerable interest. He finds that the organism reacts to stimuli of harmful or threatening character by an increased activity. Among the manifestations of this are the psycho-galvanic reflex and a general increase of muscle tone. On the other hand, inaction or diminished activity seems to be the typical response to benign stimuli. These observations fall into line with the physiological conception of immobility which is put forward here.

Hysteria and the reaction by immobility. If this view of immobility be correct, Rivers's suggestion that hysterical phenomena are modified reactions to danger by immobility cannot be adequate or even accurate. Paralysis is not comparable with the active maintenance of an attitude. Moreover, the occurrence of motor convulsions as a manifestation of hysteria cannot be included within such an hypothesis. Rivers recognizes this and therefore assumes that the hysteria of civil life, concerning which he quite frankly disclaims any experience, may in part be induced by reactions to the sex instincts, which are convulsive in type. A second assumption is thus rendered inevitable regarding the character of the hysterical fits of

soldiers. Rivers believes these 'are very different from those of civil practice. The patient lies motionless and silent, and in a state quite consistent with a relation to the instinct of immobility.' Therefore, he proceeds to argue, 'it would conduce to clearness of thought and to successful practice, if two distinct varieties of hysteria were recognized, the two differing in the nature of their aetiology. It may then become apparent that two very different concepts have been confused under the heading of hysteria.'

We cannot believe that either clearness of thought or a rational therapy is to be achieved by distorting the facts of clinical observation in this procrustean bed of theory. Few neurologists, with both civil and war experience, will be found to admit that the 'hysterical fits' of soldiers differ in any essential respect from those seen in civil practice. Violent convulsive seizures were relatively common in the writer's experience in a particular field of war. Certainly apparent immobility, in Rivers's sense, was sometimes seen, either as the sole manifestation of a 'fit', or more commonly as the terminal phase of a powerful general convulsion. But careful examination revealed that active innervation of muscles was the rule in these cases, as attempts at passive movement or at opening the eyelids soon demonstrated.

Manipulative activity. In his conception of manipulative activity as an instinctive or innate reaction, we find it quite impossible to follow Rivers. Manipulative activity is the phrase used to describe the normal reaction of the healthy man to danger. Man 'responds by a special kind of activity, often of a highly complex kind, whereby the danger may be avoided or overcome'. As examples of this, he notes the use of weapons, motor-cars, or aeroplanes. A characteristic feature of this mode of response is the absence of affect, for fear would prevent the carrying out of the skilled devices employed by man in the face of danger. Rivers says 'it needs a prolonged course of training to enable a man to fight, whether with his fists or with weapons, and yet preserve his composure so that he can discriminate the movements of his enemy and adjust his own actions accordingly . . . this training consists in putting the crude actions of the primitive instinct of aggression under subjection to carefully discriminative and chosen actions based on intelligence'. This, then, is the reaction of the normal man to danger, an admirable description of purely intelligent and discriminating behaviour, which Rivers nevertheless classes with the innate instinctive reactions. That this is no instinctive reaction would accord with the suggestion that it is not accompanied by the corresponding affect. The flight 'from bough to bough' of our (very improbably) arboreal ancestors is the germ from which man's manipulative activity is supposed to have arisen, and Rivers draws a great distinction between this and a purely terrestrial form of flight. He considers that while running is purely blind and impulsive, arboreal progression demands more finely adjusted co-ordination of hand and eye, and the suppression of the tendency to the blind impulsive flight of ground-dwelling ancestors. It is difficult to detect any fundamental difference between flight through a jungle and flight through trees above ground. Quite possibly the latter demands finer co-ordination, but both are innate reactions, and as such are equally removed from the highly discriminative fashion in which man may outwit his enemies, using flight or aggression, immobility or some combination of skilled purposive movements, or finally some piece of mental agility, all of which are dictated

by his judgement, which may or may not induce him to employ some simple reaction such as flight.

In conclusion, while admitting the fascination of Rivers's views, we believe that his book should be regarded rather as a bold essay in speculation, as a biological allegory, rather than as a contribution to knowledge. Viewed in the former light it is delightful to read, but accepted as the latter we fail to see in what respect it can be helpful. F. M. R. W.

Mott, F. W., and **Such, M. P. y. Further pathological studies in dementia praecox, especially in relation to the interstitial cells of Leydig.** *Proc. Roy. Soc. Med.*, 1922, **15** (Sect. Psychiat.), 1.

The conclusions reached from the investigations recorded in these papers are that prior to birth the interstitial cells, which predominate in the interstitial tissue making up the greater part of the testes, act as sexual determinants. After birth they undergo a regressive atrophy and disappear. The lipoid contained in these cells and lying without them is probably nutritive material for the growing seminiferous tubules and disappears as these develop. At puberty and adolescence, when the seminiferous tubules have greatly increased in size, abundant mature interstitial cells are present containing lipoid granules. They continue to mature and to decay and to be replaced by others during life. The origin and function of the interstitial lipoid are discussed. The microscopic appearances of these cells in 27 cases of dementia praecox are described. Both seminiferous tubules and interstitial cells undergo regressive atrophy in this disease. The testicular changes found in general paralysis of the insane are contrasted with those seen in dementia praecox (cf. *Medical Science*, 1922, **5**, 332). F. M. R. W.

Lhermitte, J., et **Fumet.** Syndrome thalamique avec autopsie. [**Case of thalamic syndrome with autopsy.**] *Rev. neurol.*, 1921, **28**, 1259.

A case of right hemiplegia of sudden onset without loss of consciousness in a woman of 74. She was first examined on the third day of her illness. There was a complete right hemiplegia, as far as the limbs were concerned, with slight affection of the lower part of the face on the affected side, but no deviation of the tongue. The limbs showed slight but definite spasticity. There was no hemianopia. There were no abnormal subjective sensations of any kind, but examination revealed grave disorders of sensation. Cutaneous sensibility to touch, pain, and temperature were completely lost over the paralysed limbs, and impaired over head and trunk on the right. The right corneal reflex was abolished. Vibration sensation and the sense of position were completely abolished in the right limbs. Reflexes: the right abdominal reflexes were absent, and an extensor type of plantar response with flexion of the limb was obtained from the right foot. The tendon reflexes were equal and normal on the two sides. The mental state was practically normal, the patient was well oriented and answered questions rationally.

During the following days the motor symptoms rapidly improved, but the sensory disorders cleared up more slowly. In about two months a stationary condition was reached. Movements of considerable amplitude could be carried out by the right limbs, but they were very ataxic. Cutaneous sensibility had also returned over the right limbs, but stimuli were not accurately localized. In the right arm, however, there remained loss of

the sense of position and of appreciation of size and form of objects held in the hand. Vibration sensation was also still very defective. At no time were any subjective sensory disturbances noted, and there is no mention made of abnormal reaction to cutaneous sensory stimuli. From this time on till death from broncho-pneumonia in the fifth month of the illness, the mental state remained sufficiently good for sensory examination, and the authors state that 'it is possible to say definitely that at no time were there any subjective sensory disturbances, no spontaneous pain, sense of weight, or formication in the affected parts'. In short, the case presented the thalamic syndrome without the painful subjective features. Examination of the brain revealed integrity of the cortex cerebri and brain-stem. The solitary lesion was an old haemorrhagic focus localized precisely in the postero-lateral zone of the thalamus, not involving the pulvinar, the thalamic radiations, or the zone of Wernicke. Histological examination had not been completed at the time of publication. This localization and limitation of the lesion explain the rapid improvement of the motor symptoms and the integrity of vision. The authors find it difficult to explain 'the complete absence of spontaneous pain and of unpleasant over-reaction to certain forms of cutaneous stimulation, which dominate the clinical picture in some thalamic cases, notably in a case earlier recorded by them.

It will be remembered that these subjective sensory phenomena and a characteristic over-reaction to certain forms of sensory stimuli are the basis of the theory of thalamic function formulated by Head and Holmes.

F. M. R. W.

Marie, P., Crouzon, O., et **Bouttier** (1). Le tartrate borico-potassique et la médication borée dans le traitement de l'épilepsie. [**Potassium boric tartrate and boric medication in the treatment of epilepsy.**] *Bull. Acad. de méd.*, 1920, **83**, 504 ; *Presse méd.*, 1920, ii, 713.

Marie, P., Crouzon, O., et **Bouttier** (2). De la nécessité de vérifier la pureté du tartrate borico-potassique dans son emploi contre l'épilepsie. [**The necessity of assuring a pure preparation of potassium boric tartrate for the treatment of epilepsy.**] *Rev. neurol.*, 1921, ii, 209.

Bégnard, A. Le traitement de l'épilepsie par le tartrate borico-potassique. [**The treatment of epilepsy by potassium boric tartrate.**] *Thèse de Paris*, 1920. (*Rev. neurol.*, 1921, ii, 1042.)

These authors all claim good results from the treatment of epilepsy by means of potassium boric tartrate in daily doses of three grammes (approximately 45 grains) in aqueous solution. According to Pierre Marie, Crouzon, and Bouttier, the results are at least as good as those obtained from bromide treatment, and are not associated with the unpleasant features of bromism, acne, gastro-intestinal disorders, or mental depression. The compound appears to act differently from the bromides, which depress the activity of the nervous centres. Potassium boric tartrate does not have this effect, and is more effective than other boric salts. It is equally valuable in children and in adults, and produces a diminished frequency and violence of the fits, leading in some instances to their cessation. In other instances fits are replaced by transient dimming of consciousness, and when the latter represent the malady they are often reduced to momentary sensations of malaise. Focal epilepsy seems equally amenable. The authors emphasize the importance of using pure preparations of the compound, and

they appear to have found that the majority of specimens obtained at random from retail druggists are extremely impure.

Bégnard records in his thesis the results of his trial of the salt, and these agree with the experiences of the authors quoted above.

In Squire's *Companion to the British Pharmacopoeia*, 1916 (p. 1107), this substance is described as tartarus boraxatus, or soluble cream of tartar. The proportions of the French compound are potassium bicarbonate, 10; tartaric acid, 10; boric acid, 5. It is a white amorphous powder, soluble in its own weight of water. F. M. R. W.

Stopford, J. S. B. The arteries of the pons and medulla oblongata. *J. Anat.* 1915–16, **50**, 131 and 255; 1917, **51**, 250.

In these three papers are discussed (i) the gross anatomy of the arteries of the pons and medulla, (ii) their distribution to the nervous system, and (iii) the clinical application of parts I and II. The vessels of 150 brains have been examined and form the material of the papers, which are of fundamental importance to the neurologist in dealing with vascular lesions of the brain-stem. They contain a vast amount of new and exact information on the blood-supply of the various structures in the pons and medulla. From their nature they are not capable of being reduced to a useful summary, and the purpose of the present note is to draw the attention of clinicians to a source of information without which no brain-stem syndrome of vascular origin can be adequately worked out. F. M. R. W.

PATHOLOGY

Greppi, S. Ricerche sperimentali sulla biligenesi. [**Experimental investigations on biligenesis.**] *Sperimentale*: *Arch. di biol.*, 1921, **75**, 485.

Experiments were made in dogs by means of injections of toluylenediamine, and led to the conclusion that experimental haemolytic jaundice is due to three factors, hyperhaemolysis, intrahepatic hyperbiligenesis, and pleiochromism. C. d. F.

Veit, B. Entzündungsvorgänge bei Kaninchen, die durch Benzol aleukocytär gemacht worden sind. [**Inflammatory processes in rabbits rendered aleucocytic by means of benzol.**] *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1921, **68**, 425.

The observation of previous authors that benzol has a strong leucotoxic power and destroys the white corpuscles of the circulating blood and haematopoietic organs is fully confirmed. Large and equal doses of benzol act in a more rapid and intensive manner than small, gradually increasing ones. Histological alterations of parenchymatous organs other than the haematopoietic ones do not appear to be brought about by benzol poisoning. If after having obtained a very high degree of leucopenia the benzol treatment is stopped and cultures of streptococci and staphylococci are injected intravenously into the poisoned animals, no increase in the number of white

corpuscles of the circulating blood is observed before the third day. The first kind of leucocytes to reappear in lymphoid and myeloid organs as a reaction to such experimental infections are the small lymphocytes. In the heart and kidneys multiple abscesses are found, but these entirely lack the typical inflammatory cell, the polymorphonuclear leucocyte, viz. they are formed of necrotic material only. The reactive manifestations observed in haematopoietic organs after experimental septicaemias in rabbits rendered aleucocytic with benzol appear to prove the truth of Weidenreich's opinion that the small lymphocyte is the undifferentiated mother-cell of all blood elements. C. d. F.

Hellman, Torsten J:son. Studien über das lymphoide Gewebe. Die Bedeutung der Secundärfollikel. [**Studies on lymphoid tissue. The significance of secondary follicles.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 333.

According to a theory of Flemming, secondary follicles are the most important centres of production of lymphocytes. In the present paper an attempt is made to show that Flemming's theory does not rest on a quite sound basis, and that it does not satisfactorily explain many observations regarding the production of secondary follicles. By assuming instead that the latter represent foci or centres of reaction against either bacteria or toxic products, or other materials penetrated into the lymphoid tissue, the formation of secondary follicles in many different pathological processes becomes quite intelligible. C. d. F.

Cevario, L. Sulla patogenesi della morte per ustione. [**On the pathogenesis of death from scalds.**] *Pathologica*, 1921, **13**, 12 and 281.

Investigations were carried out by means of healthy white rats joined in pairs by lateral coeliostomy. One of each pair underwent experimental scalding of different quality, intensity, and extension. The blood, haematopoietic organs, and central nervous system of both of them were then histologically examined. As regards the blood and haematopoietic organs the alterations changed in intensity according to the degree and number of scalds as well as according to the length of time through which it was possible to keep the animals alive after each experiment. But they did not essentially differ from those previously described by other authors after experimental scalding of single animals. The alterations of the central nervous system (cerebrum, cerebellum, and spinal cord) were on the whole characterized by intense chromatolytic changes similar to those seen after acute experimental intoxications and infections. In addition, frequent pneumonic and nephritic changes were seen. The interest of these observations, however, does not lie in the alterations themselves but in the fact that they were found to be equally intense and widespread in both animals of each Siamese pair. This justifies the suggestion put forward by the author that in consequence of scalding a toxic substance is produced to which the alterations of the blood, haematopoietic organs, and central nervous system of the scalded and non-scalded animals are essentially due. One may add that the results of Morpurgo's experiments, to which reference has already been made (*Medical Science*, 1922, **6**, 138), are in favour of this supposition. C. d. F.

Lusena, M. Studio sperimentale sulla trasfusione del sangue. [**Experiments on blood transfusion.**] *Sperimentale*: *Arch. di biol.*, 1921, **75**, 461.

The intravenous injection into rabbits of a moderate quantity of their own arterial blood, obtained a few minutes before being injected, causes in them a rapid diminution of the haemoglobin content and number of red blood corpuscles. Some of the rabbits are killed by this acute haemolytic anaemia, others recover. In a few cases the haemolytic phenomena are preceded by a transitory hyperglobulia. Citrated blood is in general less injurious than defibrinated blood. The histological investigation of the haematopoietic organs of the treated animals only shows a deposition of pigment and a remarkable histolysis of red blood corpuscles. These appear sometimes in sections of blood-vessels as clogged together in a rather peculiar manner. Why the blood should acquire such a toxi-haemolytic property simply in consequence of having been abstracted from the circulation for a few minutes remains entirely obscure, particularly because the treatment it must undergo before being re-injected does not appear to explain satisfactorily the severe symptomatology observed. C. d. F.

Guidi, F. Nuove ricerche sulla morfologia e sul comportamento degli elementi costitutivi della guaina mielinica nelle degenerazioni secondarie. [**New investigations on the morphology and behaviour of the constituent elements of the medullary sheath during secondary degenerations.**] *Riv. di patol. nerv.*, 1921, **26**, 1.

According to the author the myelin sheath of central nerve-fibres consists of a reticular stroma and of a fat-like material deposited within the meshes of the stroma under the form of minute spheres or granules. In secondary degenerations experimentally produced in spinal cords of rabbits by means of extirpation of the sciatic nerve, the granular portion of the medullary sheath of the affected fibres appears to undergo peculiar metachromatic modifications and to disappear sooner than the reticular or alveolar stroma. In course of time also this last disappears, both the granular and sustaining portions passing through phases characterized by fragmentation into irregular pieces, and fusion of the fragments into clumps. These break up finally into a detritus which is eliminated through phagocytes. Investigations were carried out chiefly by means of slight modifications of Besta's ammonio-chloride of tin methods, for which see the *Microtomist's Vade-Mecum*, 1921, 8th ed., p. 448. C. d. F.

Guerrini, G. Ricerche sulla avitaminosi. [**Investigations on deficiency diseases.**] *Ann. d'ig.*, 1921, **31**, 597, and *Pathologica*, 1921, **13**, 447.

If pigeons are fed with rice first sterilized in autoclave at 150° C. for 80 minutes and then re-integrated with the microbes forming the normal bacterial flora of the unpolished grain the symptoms of deficiency disease are more severe than in the case of pigeons fed on simply sterilized rice. This greater severity of symptoms cannot be referred only to an increased virulence of the added germs. As shown by Petragnani (*Igiene mod.*, 1921, **14**, 141), pigeons affected by deficiency disease are no longer resistant to the infection with *B. chauvoei*. This loss of natural immunity does not appear connected with a quantitative food deficiency, but with the fact that pigeons affected by deficiency disease appear no longer capable of producing anti-

bodies such as agglutinins. The diarrhoea of pigeons showing symptoms of deficiency disease is connected with a more virulent and strongly developed intestinal flora in which the *B. coli* predominates. C. d. F.

Luzzatto, R., e Levi, A. Lesioni disseminate del sistema nervoso nell' avvelenamento per una base grassa non satura. [**Disseminated lesions of the nervous system due to poisoning with an unsaturated fatty base.**] *Riforma med.*, 1921, **37**, 1148.

This is a brief but rather interesting preliminary note on nerve lesions caused by vinylamin (C_2H_5N). This substance, the molecular constitution of which is still a subject of discussion, has already occupied the attention of various authors (Ehrlich, Levaditi, Gabriel, Markvald, Luzzatto), because of its toxic action manifesting itself after a period of incubation lasting from 6 to 24 hours, and because one of its most important effects, as was pointed out by Ehrlich, is a necrosis of the renal papillae. Luzzatto and Levi have now observed that doses of 0·005 to 0·008 gm. per kilo of pure neutral hydrochlorate of vinylamin, when injected either subcutaneously, intravenously or intraperitoneally into rabbits, are sufficient to cause disseminated lesions of the white substance of spinal cord. Such lesions are not rendered visible by Marchi's method or its modification, but can be shown by means of Donnaggio's method for positive staining of nerve-fibres in the initial phase of primary degeneration. If even smaller doses of the same substance (0·001–0·003 gm. per kilo) are injected intrarachideally the toxic effect also begins to manifest itself after a period of incubation and the animals may survive for about 4 days, at the end of which the same disseminated primary degeneration of the medullated fibres of spinal cord can be observed. But the lesions are in this case more widespread and intense in character, and very much remind one of the plaques of disseminated sclerosis, except for the absence of the proliferation of neuroglia, the animals not surviving long enough for a manifestation of this kind. C. d. F.

Bedson, S. P. Blood-platelet antiserum, its specificity and rôle in the experimental production of purpura. *J. Path. & Bacteriol.*, 1922, **25**, 94.

Continuing his work on antiplatelet serum (*Medical Science*, 1922, **5**, 496, 525), the author shows that of various antisera prepared by immunization with blood-elements (cellular or otherwise) antiplatelet serum alone produces purpura, a result which is independent of any haemagglutination. An extensive though temporary reduction in the number of blood-platelets in the circulating blood of the rabbit does not give rise to purpura. Apparently there is an added factor which the author conceives to be a toxic action on the vascular endothelium. By direct observation of the mesenteric vessels under the microscope it would seem that in purpura produced by the injection of antiplatelet serum the capillary endothelium is first of all damaged, and later, when the platelets have been greatly reduced in number in the circulating blood, a leakage of red cells takes place through the capillary wall into the surrounding tissues. W. B.

Stewart, M. J. **Malignant sacrococcygeal chordoma.** [**B.**] *J. Path. & Bacteriol.*, 1922, **25**, 40.

A well-reported and illustrated case of the rare tumour known as malignant chordoma (Ribbert) which arises from remnants of notochord and

is met with chiefly near the spheno-occipital synchondrosis (clivus Blumenbachii) and in the sacrococcygeal region. The patient, a man aged 65, had a slow-growing tumour over the coccyx, and it attained the size of an orange. Five years after excision it recurred in the left buttock, and three years later a mass appeared over the right scapula. These also grew slowly and, while the scapular mass remained discrete and encapsuled, the tumour in the left buttock caused great destruction of the femur and iliac blade on that side, death occurring 11 years after removal of the primary growth. The histological characters of the tumour and the physaliphorous cells are described. A complete bibliography of all the known cases accompanies the paper. W. B.

Daly, I. de B., and Starling, E. H. On the effects of changes in intraventricular pressure and filling on the ventricular rhythm in partial and complete heart-block. *Brit. J. Exper. Path.*, 1922, **3**, 1.

(1) In confirmation of other observers it was found that after complete division of the auriculo-ventricular bundle, acceleration of the idio-ventricular rhythm can be evoked by stimulation of the cardio-sympathetic nerves. (2) In the heart separated altogether from nervous impulses, as in the heart-lung preparation, a rise of arterial pressure, or increased inflow into the heart, frequently causes increase in the idio-ventricular rhythm after complete division of the auriculo-ventricular bundle. (3) It cannot yet be decided whether this result is due to the stimulating effects of increased tension or increased stretching of the ventricular wall, or to a direct irritant effect of the stretching on the recent lesion in the neighbourhood of the auriculo-ventricular bundle. Reasons are given for believing that the latter is the more likely explanation. (4) After partial division of the auriculo-ventricular bundle, a rise of arterial pressure or increased filling may cause the block to become complete, the block becoming once more incomplete when the pressure or filling is reduced to its previous value. P. F.

Russell, B. R. G. The carbohydrate metabolism of surviving mouse tissues and tumours. *Brit. J. Exper. Path.*, 1922, **3**, 51.

The low respiratory quotient observed with slowly-growing transplanted tumours is not attributable to their incapacity of burning glucose. Mouse tumours and tissues appear capable of dealing with the common sugars in a very similar manner, provided the sugars are supplied directly. Differences in the quantity of sugar within the cells is a probable explanation of the variations in the carbohydrate metabolism of tumours growing at different rates. P. F.

Harrison, G. A. On urea tests of renal function. *Brit. J. Exper. Path.*, 1922, **3**, 28.

(1) The provocative urea concentration test in 400 cases was found most useful. The following additional points should be noted: (*a*) withhold fluid 6 to 12 hours beforehand; (*b*) measure volume of urine each hour; volume first hour should not exceed 150 c.cm., second or subsequent hours 100 c.cm.; if volumes greater, diuresis occurs; when results below 2 per cent. they do not necessarily imply inefficient kidneys; (*c*) occasionally diuresis

unavoidable when other tests are required; 1 c.cm. pituitrin checked diuresis in one case of diabetes insipidus; (*d*) 15 gm. not always sufficient; (*e*) proteinuria exceeding 0·4 per cent. may introduce errors, especially when urea close to 2 per cent.; (*f*) 'normal,' above 2·5 per cent., signifies more than quarter kidney tissue functioning on day of test. Check figures below 2·5 per cent. by blood urea. (2) Blood urea may be affected by diet. (3) Urea concentration factor (U.C.F.) is defined thus:

$$\frac{\text{mgm. urea per 100 c.cm. urine (third hour)}}{\text{mgm. urea per 100 c.cm. blood (middle third hour).}}$$

Sometimes a 'normal' urea concentration in urine may be due to high blood-urea. 'Normal' values of U.C.F. uncertain. U.C.F. repeated at intervals assists prognosis. U.C.F. guide to rational treatment of oedema in nephritis by urea.

P. F.

Drew, A. H. A comparative study of normal and malignant tissues grown in artificial culture. *Brit. J. Exper. Path.*, 1922, **3**, 20.

Continued growth of normal and tumour cells *in vitro* is only obtained in the presence of substances so far only found in embryonic extracts. A salt mixture in which the calcium is present in the colloidal state can, with the addition of embryo extract, replace plasma for this work. The degree of differentiation shown by cultures of normal and malignant tissues is partly conditioned by the accompanying growth of the stroma. The stroma behaves in culture like embryonic tissue rather than like the adult tissues from which it is derived. P. F.

Elliot, W. E., Crichton, A., and Orr, J. B. The importance of the inorganic constituents of the food in nutritional disorders. I. Rickets in pigs. *Brit. J. Exper. Path.*, 1922, **3**, 10.

Rickets develops in pigs deprived of access to earth or other mixtures of minerals, and fed only on grains and certain other foodstuffs which contain little vitamin A and in which the mineral matter either in amount or in composition is not suited to the requirements of the animal. The adjustment of the mineral content of the food to the needs of the animal by the addition of a calcium-rich mixture of salts prevented the occurrence of the disease even though no additional vitamin A was added. The addition of vitamin A factor without the adjustment of the mineral matter did not prevent the development of the signs of experimental rickets. The importance of a sufficiency of the essential inorganic constituents of the diet and of the proper ratio of these to each other is emphasized. The pig seems to be little susceptible to deprivation of vitamin A factor compared with the rat. The beneficial effect of cod-liver oil on the rate of growth and the general health became apparent towards the end of a three-month experimental period. No evidence of the rickets syndrome was found to develop on a diet deficient only in vitamin A factor. P. F.

Mattirolo, G. Sulla sclerosi primitiva dell' arteria polmonare. [**On primary atherosclerosis of pulmonary artery.**] *Arch. per le sc. med.*, 1921, **44**, 125.

Description of another case of primary atherosclerosis of pulmonary arteries identical with that recently published by Gamna (see *Medical Science*, 1922, **6**, 134, and the references therein quoted). C. d. F.

Da Fano, C. (1). **Changes of Golgi's apparatus in nerve-cells of the spinal cord following exposure to cold.** *J. Nerv. & Ment. Dis.*, 1921, **53**, 353.

Da Fano, C. (2). **On Golgi's apparatus of transplantable tumour-cells.** [**B.**] *Scient. Rep. Imp. Cancer Res. Fund.*, 1921, **7**, 67.

The investigations on the alterations of Golgi's internal apparatus in the nerve-cells of the spinal cord of small animals exposed to cold for different periods of time were carried out by means of the author's modification of Cajal's uranium nitrate method. This modification, known as the cobalt nitrate method, was first communicated to the Physiological Society (*J. Physiol.*, 1920, **53**, xcii) and then fully described in the *J. Roy. Micr. Soc.*, 1920, p. 157. The conclusions reached are: protracted exposure of small animals to a moderate degree of cold is sufficient to cause peculiar changes of Golgi's internal apparatus in the nerve-cells of the dorsal horns, intermediolateral and middle cell columns, and grey matter surrounding the central canal. Such changes are characterized by an unusual prominence in the whole apparatus and of its constituent parts, which show a tendency to occupy a tight perinuclear situation. In more affected specimens the apparatus gradually loses its characteristic structure and becomes transformed into irregular and variously arranged masses and pieces. These alterations are accompanied by an appearance of canaliculi and spaces similar to those generally spoken of as Holmgren's trophospongium. If the exposure to cold has been such as to lower considerably the normal temperature of the animals experimented upon, the same apparatus undergoes a further form of almost complete disintegration.

For his research on the Golgi apparatus in transplantable tumours of the mouse, rat, and guinea-pig, the author had resort to his cobalt nitrate method, to Golgi's arsenious acid, and Cajal's uranium nitrate methods, as well as to a modification of an unpublished process devised by Veratti for the demonstration of mitochondria. For this modification the term 'potassium antimoniate method' is proposed. The results obtained are illustrated by 13 plates and summarized in the following conclusions: the presence of an internal apparatus is a constant feature of the healthy cells of all transplantable tumours, within which it appears with aspects changing from one to the other growth, but characteristic of almost all of them. As regards structure, intracellular situation, and evolutional changes, the apparatus of transplantable tumour-cells resembles that described by other authors either in normal or pathological tissues. This appears to prove once more that no essential differences exist between the new growths of small laboratory animals and those of the human being, and strengthens the belief that, apart from the greatly increased power of multiplication, tumour-cells are in every way similar to those forming normal tissues. The characteristic aspect of the apparatus of given tumour-cells is independent of the methods used for its demonstration, is maintained throughout many generations of the same tumours, and reappears even in the case of cells undergoing various degenerative changes. Hence the inference that the different structural types of the apparatus are not the result of some coagulating action of fixing reagents or of a hypothetical capriciousness of the silver impregnation, but, in part at least, the expression of a mode of being in the living cells. The apparatus is frequently stained in tumour-cells at the same time as other intracellular formations similar to Meves's chondriosomes. This confirms the existence of a certain analogy in the chemical composition of the

two structures, which otherwise entirely differ in aspect, intracellular situation, and behaviour during altered life conditions. As in the case of normal tissues, the apparatus of mitotically dividing cells breaks up into rod-like shapes and fragments which are distributed between the daughter-cells and rebuild a new apparatus in each of them. The apparatus gains in size and complexity of structure in hypertrophic elements, and it may acquire an individuality of its own in multinucleated giant cells. It undergoes disintegrative processes which appear to be strictly connected with degenerative cell changes of various kinds. It cannot, therefore, be identified with a fixed system of canaliculi, but it should be considered as a minute cell organ, the function of which is still unknown. C. d. F.

Penfield, W. G. The Golgi apparatus and its relationship to Holmgren's trophospongium in nerve-cells. *Anat. Record*, 1921, **22**, 57.

For previous work on this subject by the same author see *Brain*, 1920, **43**, 290. Investigations were carried out by means of Cajal's uranium nitrate method. For counter-staining he finds it particularly useful to immerse untoned sections in a dilute solution of polychrome methylene blue for 1 to 4 hours, this being followed by passage through alcohols of increasing strength and differentiation in absolute alcohol. By this method also Holmgren's trophospongium is sometimes stained. But for the study of the relationship between the latter and Golgi's apparatus Penfield prefers to make drawings of the apparatus from certain selected cells, subsequently removing the cover-slip and bringing the slides through graded alcohols into 5 per cent. iron alum for 12–24 hours. This removes all silver from the cells as well as the counter-stain, and at the same time mordants the tissues for further staining with iron-haematoxin. If the proper amount of differentiation has been secured of the particular cells already drawn, the trophospongium is found stained with great detail. The results obtained are summarized in the following conclusions: In neurones the apparatus reacts to axone section in a specific manner. There is no similar response on the part of Holmgren's trophospongium. The two structures may be demonstrated independently in the cytoplasm of the same neurone, either successively or simultaneously. Occasionally there appears a close anatomical relationship between parts of the apparatus and of the trophospongium, which may indicate an intimate association of function. Further work upon the Holmgren canals is required clearly to demonstrate the developmental stages and in fact their existence *ante mortem*. C. d. F.

Bernucci, F. Sul comportamento degli epiteli secernenti renali rispetto alle sospensioni di sostanze finamente granulose iniettate in circolo. [**Behaviour of secretory epithelia of kidney after intravenous inoculations of suspensions of finely granular substances.**] *Morgagni*, 1921, **64**, 316.

Experiments were carried out by means of suspensions in physiological salt solution of methylene blue, indigo-carmine, and China ink. These were injected intravenously into healthy guinea-pigs and into others in which a subacute poisoning had been caused by corrosive sublimate. The results obtained were: Finely granular materials introduced into the circulating blood of healthy animals accumulate in the epithelial cells lining the convoluted tubules and ascending branch of Henle's loops. The granules generally collect round the nucleus and in the part of the cytoplasm turned

towards the canalicular space. The cells containing granules are somewhat larger than normal, and their cytoplasm, while no longer possessing its usual rod-like aspect, shows dense areas alternating with rarefied ones. Not all cells of convoluted tubules ingest granules at the same time and in the same quantity. During subacute intoxications affecting the kidneys this power of ingesting granules is remarkably diminished or abolished.

C. d. F.

Galassi, C., e Conti, L. Sul ricambio emoglobinico nella tubercolosi. [**Haemoglobin exchange in tuberculosis.**] *Boll. d. Soc. med.-chir. di Pavia*, 1921, **34**, 65.

In the blood of all patients examined no elements of the embryonic series were seen. The globular resistance appeared on the whole diminished. The number of red corpuscles and the haemoglobin content were often found unaltered. However, there is in tuberculosis a noticeable and continuous destruction of red blood corpuscles, as shown by the quantitative determination of bilinogen in urine and faeces at the same time. This destruction is not perceived by ordinary methods for the determination of haemoglobin because parallel with it there is an equally continuous and compensating neoproduction of red corpuscles. C. d. F.

D'Abundo, E. Focolai subcorticali cerebrali e loro effetti anche in rapporto con le manifestazioni idrocefaliche. [**Cerebral subcortical foci and their consequences also in relation to hydrocephalus.**] *Riv. ital. neuropat.* (&c.), 1921, **14**, 225.

Experiments were made on kittens and puppies and led to the following conclusions: In consequence of local and limited subcortical destructions of white matter, cavities are generally found limited by an inflammatory infiltration which, in recent cases, may continue into the overlying convolutions. Such cavities either permanently remain in the form of cysts or disappear through a process of cicatricial retraction which is recognized only by microscopic examination. This reveals also an atrophy of the surrounding nerve-fibres, associated with a moderate hypotrophy of the convolutions from which the fibres originate. Apart from this fact, experimental subcortical destructions of the white substance do not modify the external aspect of the affected hemisphere even when the lesion is extended enough to reach to lateral ventricle. The cerebral convolutions appear flattened only when the destructions have such an extension as to be the cause of a remarkable degree of intraventricular hydrocephalus with increased endocranial pressure. When an hydrocephalic condition is brought about in one hemisphere the opposite one also becomes affected, though in a less noticeable manner. With reference to human pathology these experiments show that subcortical lesions represent points of permanent organic weakness and emphasize the necessity for carefully looking for them in all obscure nervous syndromes. C. d. F.

Marassini, A. Contributo sperimentale alla fisiopatologia della pressione arteriosa del sangue. [**Experimental investigations on the physio-pathology of arterial blood-pressure.**] Note I. *Arch. di fisiol.*, 1920, **18**, 21. Note II. *Arch. per le sc. med.*, 1921, **44**, 143.

A compensating intravenous injection of 0·7 per cent. NaCl warmed at 38° C. is not sufficient to restore to the former level the blood-pressure

lowered in dogs by means of a great and rapid abstraction of blood. However, the height reached by the blood-pressure in such conditions, though lower than the normal, is sufficient to maintain life. If the blood-letting is repeated many times and the blood loss is each time compensated with an equal volume of 0·7 per cent. NaCl injected through the jugular vein, the average blood-pressure becomes lower each time. If, after blood-letting, injections of physiological salt solution are made in such a quantity as to increase the total mass of the circulating fluid, the blood-pressure may temporarily reach very high levels, but soon descends to one which is out of proportion to the quantity of injected fluid. Life, and a return to normal conditions are possible even in such cases. The lower the haemoglobin index and the higher the blood-pressure the greater is the quantity eliminated from circulation of the fluid injected for compensating a great loss of blood.

If the blood abstractions are moderate in quantity and frequently repeated, and the blood loss is each time compensated with an equal volume of physiological salt solution, the average blood-pressure undergoes a progressive diminution. Under such conditions the partial successive diminutions are much less noticeable at the beginning of the experiment than in the following periods, when they become quite remarkable, similarly to what happens after moderate and repeated blood-letting non-compensated with injections of physiological salt solution. The average blood-pressure after having been brought to a very low level may remain at that for a long time, when it is possible to proceed to a further abstraction of blood and to its substitution with physiological salt solution. However, the dilution of the blood is always very small in comparison to the volume of the fluid introduced. This is continuously eliminated from circulation just as in the case of great abstractions of blood. C. d. F.

BACTERIOLOGY

Paranhos, U. Un nuovo metodo di sterilizzazione dei prodotti organoterapici. [**New method of sterilization of organo-therapeutic products.**] *Ann. d'ig.*, 1921, **31**, 620.

By means of an isotonic solution of sodium fluoride, organo-therapeutic products can be obtained containing 0·10 gm. of the given organ and 1 mgm. of NaF_2 to every c.cm. of the final product. Preparations of this sort remain indefinitely sterile and do not give rise to any trouble when injected into man. C. d. F.

Sieke, F. Phenolbildung durch Bakterien. [**The formation of phenol by bacteria.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 214.

The author examined a large number of cultures for phenol production and studied in particular a *B. coli phenologenes* and a *B. paracoli phenologenes*. The best medium was found to be one consisting of tyrosin 0·3 gm., asparagin 5·0, ammonium lactate 5·0, magnesium sulphate 0·2, potassium phosphate 2·0 and distilled water 1,000 gm. The presence of phenol was demonstrated by the blue Berthelot-Lex reaction (p. amidophenol in alkaline

reaction in the presence of sodium hypochlorite), which depends on the formation of indophenol. *Bacillus coli phenologenes* yields deep red colonies on endo agar and actively ferments glucose and lactose. In the case of *B. paracoli phenologenes* the endo colonies were white and lactose fermentation was slight. The phenol-splitting property of both types was constant. Immune sera were prepared and showed in agglutination tests that the two phenol-forming types of *B. coli* and *B. paracoli* were agglutinogenically different from each other and from non-phenologenes strains of *B. coli*. Phenol-forming strains of *B. coli* were found in the gut in 85 per cent. of all persons examined. Phenol formation was also demonstrated in three cultures of the bacillus of fowl cholera and in two of *B. ozaenae* Perez.

W. B.

Klostermann. Ueber eiweissfreien Agar-agar. [**On protein-free agar.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 262.

The author gives an account of the sources and chemical constitution of agar, and describes a method whereby it may be made protein-free, an important point in the use of agar for performing anaphylactic experiments.

W. B.

Frieber, W. Beiträge zur Frage der Indolbildung und der Indolreaktionen sowie zur Kenntnis des Verhaltens indolnegativer Bakterien. [**Indol formation and tests for indol and the behaviour of indol-negative bacteria.**] *Centralbl. f. Bakteriol.* (&c.), Abt. I, 1921, **87**, Orig., 254.

The author discusses several instances which have been long in dispute regarding the reaction of certain bacteria to well-known indol reagents. He has also investigated the metabolism of certain bacteria which have variously been described by different observers as indol-negative and indol-positive. It has not been known whether, in the growth of indol-negative bacteria, the substance which is universally believed to be the mother-substance of indol, namely tryptophane, is not attacked and therefore gives no indol reaction, or whether this substance is katabolized to indol and the indol used up by the bacteria as soon as it is formed. For the latter view there has been some evidence, because it has been known that indol added to a nutrient medium will supply nitrogen for the requirements of bacteria and so disappear.

There are five principal reagents which have been used for the detection of indol: (1) Ehrlich's reagent—paradimethyl-amino-benzaldehyde and hydrochloric acid, which gives a red colour; (2) Salkowski reagent—sulphuric acid and potassium nitrite, which gives a red colour; (3) De Graaf's reagent—the sodium salt of 1–4 β-naphtho-quinone-sulphonic acid, which gives a brownish-blue colour becoming red when dissolved in chloroform; (4) Weyl-Legal's reagent—an alkaline solution of sodium nitroprusside, which gives a blue colour in the presence of acid; (5) Vanillin reaction—a red colour with vanillin and hydrochloric acid.

Now it has been found that *B. typhosus* with Ehrlich's test gives a negative indol reaction, whereas Jaffé found indol in 20 cultures of this micro-organism on applying Salkowski's test. Similar variations have been found with strains of *B. paracoli*. In order to throw some light on such variations, Frieber investigated certain compounds closely allied to tryptophane but differing in certain chemical groups. It is known that trypto-

phane is β-indol-alanine, i.e. it is a compound of α-amino-propionic acid (alanine) which is attached to the indol group by the carbon atom, in the 5-membered ring, which is most remote from the nitrogen atom. This carbon atom is known as β carbon atom. Frieber utilized for his tests: (1) indol in which the α and β carbon atoms were free; (2) α-methyl-indol and indol-carboxylic acid in which the α position was occupied; (3) methyl-indol, (skatole) β-indol-aldehyde, β-indol-acetic acid, β-indol-ethylamine (tryptamine), β-indol-alanine (*l*-tryptophane), synth. *d*+1 tryptophane, β-indol-glycyl-alanine (glycyl-tryptophane) β-indol-pyruvic acid and indol-acetylformic acid, in all of which the β position is occupied; (4) α and β indol-carboxylic acid, α-methyl-β-indol-alanine (α-methyl-tryptophane), indoxy-carboxylic acid and isatine. With these various compounds the author tested for indol reactions, using the 5 reagents mentioned above. The results of the tests showed that Ehrlich's reagent gives a positive reaction with indol and methyl-indol, and does not react with β-methyl-indol, indol-aldehyde, indol-carboxylic acid, indol-acetic acid, indol-pyruvic acid, tryptophane, tryptamin, α-methyl tryptophane or glycyl-tryptophane. The Salkowski reagent reacts with indol, indol-acetic acid, and indol-pyruvic acid. Weyl-Legal's reagent gives positive reactions with indol, but not with any of the other compounds tested. Vanillin reacts with indol and methyl-indol, but not with other compounds. Hence there is a fundamental difference between the four main tests. What is most noteworthy is that the chief difference between the Ehrlich and Salkowski reagents is that the former does not react with indol-acetic acid while the latter does. In order to ascertain why the varying results with cultures are obtained by the two reagents, Frieber set up a number of bacterial cultures, among them being *B. typhosus* and *B. diphtheriae*, with a synthetic medium containing tryptophane. In all cases he was able to demonstrate a positive Salkowski but a negative Ehrlich reaction. In seeking for an explanation for this behaviour he comes to the conclusion that the bacterial breakdown of tryptophane proceeds in two stages. First there is a removal of the α carbon atom with the amino group which leads to the formation of indol-acetic acid. The bacteria which are able to do this give a positive Salkowski reaction. Secondly, the indol-acetic acid is oxidized to indol, and when this occurs the bacteria yield both the Salkowski and the Ehrlich reaction. The second stage can only be preceded by the first. Indol-acetic acid itself cannot serve as a precursor of indol. He noticed that only Gram-negative bacteria are indol-positive. The Salkowski reaction is not a test for indol but for indol-acetic acid. The only practical test which is specific for indol is that of Ehrlich. *B. pestis*, *B. diphtheriae*, *B. mallei*, *B. pneumoniae*, *Staphylococcus pyogenes*, and *Sarcina* are not indol-formers, neither are *B. paratyphosus*, *B. paracoli*, and *Proteus vulgaris*. These may, however, all give a positive Salkowski reaction; hence the latter has no diagnostic significance. In order to test for indol one must rely exclusively on the Ehrlich reaction.

C. G. L. W.

Hansen, T. Overfladeaktive Stoffers Indflydelse paa forskjellige Desinfektionsmidlers bakteriedraepende Evne. [**Surface tension and the antiseptic action of disinfectants.**] *Hosp.-tid.*, 1921, **64**, 657 and 673.

The observation made by Johanne Christiansen in 1918, that a relation exists between the disinfectant action and surface tension of the alcohols,

suggested to Hansen that the antiseptic action of certain disinfectants might be enhanced by altering their surface tension by the addition of alcohol. He finds that the numerous investigations already made show a remarkable conflict of evidence, but, by scrutinizing the methods adopted, he thinks that the contradictory character of the evidence is more apparent than real. Earlier investigators may have gone astray because they did not understand the action of alcohol by itself before they studied its effects in conjunction with other substances. And they did not realize the differences in the action of alcohol upon bacteria in the moist and dry state. Hansen refers to Robert Koch's work in 1881, when he found that alcohol diminished the antiseptic action of disinfectants. He arrived at this conclusion by testing dried anthrax spores with a 5 per cent. aqueous solution of phenol and a 5 per cent. solution of phenol in absolute alcohol. After discussing these and later investigations, Hansen concludes that there is remarkable unanimity as to the inability of high concentrations of alcohol to increase the antiseptic action of disinfectants. But the evidence becomes contradictory when the action of the medium and weak solutions of alcohol is studied.

Hansen worked only with bacteria in the moist state, and he standardized a suspension of *S. pyogenes aureus* so that it should contain 2,000,000,000 to 1 c.cm. To test-tubes containing 2 c.cm. of various disinfectants kept on a water-bath at 20° C., he added 0·2 c.cm. of his suspension, i.e. 400,000,000 bacteria. The results are shown in 11 tables. A solution of 0·05 HCl destroyed the germs in 22·5 minutes, whereas this period was reduced to 7·5 minutes when 7 per cent. propyl alcohol, or 10 per cent. ethyl alcohol, or 20 per cent. methyl alcohol was added to the HCl solution. Thus by the reduction of the surface tension of the HCl solution its disinfectant action was greatly increased, and this increase was exactly the same for the three alcoholic solutions whose service tensions were the same. Acetone acted in the same way as ethyl alcohol, but saponin and peptone did not increase the disinfectant action of HCl, and glycerine considerably reduced the disinfectant action of phenol. Other disinfectants with which small quantities of alcohol were tested were perchloride of mercury, chromic acid, formalin, and boracic acid. In the case of formalin the addition of ethyl alcohol up to a strength of 15 per cent. reduced its disinfectant action, and it was not till the strength of the alcohol was raised to 40 per cent. that the formalin's disinfectant action was greater than in an aqueous solution. Hansen also used anthrax spores, employing the same technique, with this exception, that the test-tubes containing the disinfectants and spores were kept at a temperature of 37° instead of 20° C. The results were still more striking; 70 per cent. of ethyl alcohol alone could not kill these spores in 31 hours, and 0·1 HCl took between 29 and 30 hours to kill them, whereas this time was reduced to less than half an hour when the spores were subjected to combined action of 70 per cent. ethyl alcohol and 0·1 HCl. Hansen discusses the various hypotheses which might explain this phenomenon, and he points out that the increased disinfectant action obtained cannot be due simply to the addition of one antiseptic to another, for 5 per cent. alcohol has no disinfectant action by itself, whereas it definitely increases the disinfectant action of other antiseptics. Whatever the explanation, the fact remains that the addition of 10 to 20 per cent. of ethyl alcohol or of 5 to 10 per cent. of propyl alcohol increases many times over the antiseptic action of HCl, phenol, perchloride of mercury, and chromic acid. C. L.

Khaled, Z. A comparative study of bovine abortion and undulant fever from the bacteriological point of view. *J. Hyg.*, 1921, **20**, 319.

In comparative experiments the author finds that morphologically *B. abortus* and *B. melitensis* are identical. The coccoid form is not a constant feature of the cultures, and a more satisfactory generic name would be 'Brucella' (after Sir David Bruce, who discovered the microbe of Malta fever in 1886). *B. abortus* cannot be distinguished from *B. melitensis* by cultural, biochemical, or agglutination tests. From absorption tests the author concludes that *B. melitensis* may be a substrain of *B. abortus*. Dose for dose, *B. abortus* is much less virulent for guinea-pigs than *B. melitensis*, the ratio being approximately 1 : 6. In one experiment a *Macacus rhesus* immunized with *B. abortus* was protected against an infecting dose of *B. melitensis*, which in a control monkey (*M. sinicus*) produced a definite febrile state.

W. B.

Strumia, M. Sui tipi di pneumococchi dominanti nelle pneumoniti del 1920 a Torino. [**Pneumococcus types in the pneumonia of 1920 in Turin.**] *Arch. per le sc. med.*, 1921, **44**, 188.

The results obtained are summarized in the following table :

Pneumococcus.	Number of Cases.	Percentage.
I	18	64.2
II Typical	3	10.7
II Atypical	1	3.5
III or mucous	4	14.28
IV or heterogeneous	2	7.1

Out of 7 cases which ended fatally five were due to Type I, one to Type III, and one to the association of Types I and III. The general conclusions which the author draws from these results are : The findings entirely agree with the observations of American authors. The clinical course of pneumonia is influenced by the type of pneumococcus to which it is due. The determination of the pneumococcus type has a great prognostic value and should be always and systematically carried out. C. d. F.

Pane, N. Su di un metodo elettivo per isolare lo pneumococco dallo sputo e l'enterococco dalle feci e sui caratteri che differenziano i due germi. [**On a selective method for the isolation of pneumococcus from expectoration and enterococcus from faeces and the discrimination between the two germs.**] *Riforma med.*, 1921, **37**, 1147.

Conclusions : Among the non-sporogenous bacteria of the intestinal flora, enterococcus (Gram-fast intestinal diplococcus) is the most resistant to desiccation at 37°–38° C. ; among those of the oral flora, pneumococcus (septic salivary diplococcus) possesses a similar but not identical degree of resistance to the same treatment. A 1 per cent. glucose bouillon is a selective medium for both these microbes after desiccation, because the rapid acid fermentation of the medium prevents the development of concomitant spore-bearing germs. The most decisive differential character between enterococcus and pneumococcus consists in their varying degree of resistance to desiccation at 37° C. C. d. F.

Stillman, E. G. The frequency of *Bacillus influenzae* in the nose and throat in acute lobar pneumonia. *J. Exper. M.*, 1922, **35**, 7.

The author has made a large number of cultures of normal throats and noses for *B. influenzae* and has found this bacillus in 30 per cent. of the former but seldom in the latter. In patients with lobar pneumonia, however, he obtained 58 per cent. of positive results from the throat and 23 per cent. from the nose. Including cultures from the sputum, &c., *B. influenzae* was obtained from 85 per cent. of the pneumonia cases. Looking upon the differences between these figures as significant, the author advances very tentatively the hypothesis that *B. influenzae* may have some causal connexion with the onset of 'lobar pneumonia'. It may be remarked that the number of cases examined is small. P. F.

v. Angerer, C. Kritische Untersuchungen über die Ätiologie der Influenza. [B.] [**Critical researches on the aetiology of influenza.**] *Arch. f. Hyg.*, 1921, **90**, 254.

This is a critical estimate of the bacteriological results obtained in the great influenza pandemic of 1918–19 and contains extensive references to the literature chiefly in Central European countries, particularly Germany and Austria. W. B.

Bender, W. Meningitis durch Influenzabazillen. [**Meningitis due to influenza bacilli.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig., **87**, 175.

The author describes two cases of genuine influenzal meningitis and refers to 35 others in the literature. Reference is also made to the confusion of *B. influenzae* Pfeiffer and the bacillus found by Cohen (*Ann. de l'Inst. Pasteur*, 1909, **23**, 273). This organism is also haemoglobinophilic, but can be differentiated from *B. influenzae* by the fact that in small doses it produces a typical septicaemia in rabbits and guinea-pigs. True influenzal meningitis is almost exclusively a disease of children under two years and begins with gastro-intestinal or nervous symptoms. The mortality in children is about 91 per cent.; in older persons about 44 per cent. Anatomically the meningitis occurs on the convexity as well as the basis and passes to the cord. In many cases the infection is a metastatic process from a primary focus in the lung, although a primary invasion from the nasopharynx or from an otitis media is also known. W. B.

Olitzky, P., and **Gates, F. L. Experimental studies of the nasopharyngeal secretions from influenza patients. VI. Immunity reactions.** *J. Exper. M.*, 1922, **35**, 1.

Reference has already been made to the researches of the authors on the so-called *Bacterium pneumosintes* (*Medical Science*, 1921, **4**, 266, 560; **5**, 62), a filter-passing microbe which was transmitted from the nasopharyngeal secretions of influenza patients to the respiratory tract of rabbits and maintained in the latter for many generations by passage. In the present paper experiments are detailed to show that upon recovery a certain degree of immunity to the microbe has set in. This immunity may persist for fourteen months. The experiments also indicate the antigenic identity of the various strains of the active agent with each other and with *B. pneumosintes*. W. B.

Preuss, M. Epidemiologische und morphologische Influenzabazillenstudien aus dem Ende der letzten Pandemie. [**Epidemiological and morphological studies on the influenza bacillus at the end of the last pandemic.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig., **87**, 283.

The author, who carried out his investigations in Breslau, examined non-influenzal cases in two periods: (1) from June to September 1920, at the end of the pandemic, and (2) from November 1920 to January 1921, when there was almost no influenza. Of 224 persons examined in the first period influenza bacilli were found in 25 (10·3 per cent.), while in the non-epidemic second period influenza bacilli were found in only 3 out of 102 cases (2·9 per cent.). Towards the end of the pandemic, influenza bacilli were more and more rare. Over a half of those examined had had influenza previously and some were permanent carriers. W. B.

Kalkbrenner. Beiträge zur Biologie des Influenzabazillus. [**Contribution to the biology of the influenza bacillus.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig., **87**, 277.

Working in Pfeiffer's Institute the author has studied the growth factors which influence *B. influenzae.* He finds that oxyhaemoglobin added to water agar inhibits the growth, whereas the addition of oxyhaemoglobin to meat-water agar constitutes a good medium. The addition of haemin, haematin, and haematoporphyrin to meat-water agar is useless, although in the presence of streptococci and staphylococci these substances accelerate growth. In the presence of diphtheria bacilli good growth is obtained without any blood derivative at all. The growth in association with other bacteria takes place even when the latter are killed at 60° C., the accelerating factor being probably, in the author's opinion, a protein substance of fermentative character. In the presence of accelerating bacteria on blood-free media the influenza bacilli yield colonies which are atypical and the bacilli themselves longer and thicker than on blood media. W. B.

Jervell, O. Leptotrix i blodet ved et tilfælde av malign endokardit. [**A leptothrix in the blood of a case of malignant endocarditis.**] *Norsk Mag. f. Lægevidensk.*, 1922, **83**, 36.

Jervell records the case of a man, aged 20, who for several years had suffered from heart disease following an attack of rheumatic fever. An acute attack of gastro-enteritis was followed by a group of symptoms characteristic of the pyaemic form of malignant endocarditis, intermittent fever, rigors, haemorrhages into the skin, and embolism of numerous organs. The disease terminated fatally in 6 weeks. A leptothrix was repeatedly obtained in pure culture from the blood during life. It was also found on the valves of the heart and in abscesses in the spleen and heart, but not in pure culture. At first it was taken for a streptococcus; on blood-agar plates it formed greyish-white colonies surrounded by a zone of haemolysis. On ascites-agar small pin-point colonies developed. The microscope showed long chains formed of such short rods that they could almost be taken for cocci. But on culture in ascites-bouillon a luxuriant network of unusually long, non-branching chains, passing across the whole field of vision, left no doubt as to the growth not being streptococcal. The facts that no growths were obtained on gelatine, and that the germ proved innocuous to mice, rabbits, and guinea-pigs, also helped to distinguish it from streptococci.

Streptothrix and actinomyces could also be excluded, and there was little doubt about the germ being a leptothrix and responsible for the pyaemia. Jervell believes that no case of pyaemia has hitherto been traced to a leptothrix. He is doubtful as to the relation, if any, of his leptothrix to the ordinary *Leptothrix buccalis*, and he does not think it is identical with the culture grown by Arustamoff. C. L.

Fisk, Etta, and **Burky, E. L. Study on the classification of streptococci.** *J. Infect. Dis.*, 1922, **30**, 128.

The authors studied a large number of streptococci with regard to the appearance of deep colonies, in blood-agar plates of uniform composition and thickness, and the fermentation reactions in inulin, lactose, mannitol, raffinose, saccharose, and salicin. Thirdly, an attempt was made to show the relationship of serological groups to the blood-agar and fermentation groups. The authors believe that green and haemolytic types of streptococci differ culturally and agglutinogenically. The fermentation reactions are not indicators of serological groupings although inulin fermentation and the reaction in milk may possibly be of value in group determination in conjunction with the blood type. W. B.

Bell, H. H. Infection of the meninges and lungs by a species of actinomyces. *J. Infect. Dis.*, 1922, **30**, 99.

Bacteriological and pathological examination of a case of primary meningitis with pulmonary embolic abscesses due to a variety of actinomyces. The micro-organism obtained in pure culture grew aerobically and well at room temperature. Animal inoculations were all unsuccessful. W. B.

Reuss, W. Ueber einen meningokokkenähnlichen Erreger bei einem klinischen Fall von Meningitis. [**On a meningococcus-like agent in a clinical case of meningitis.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, Orig., **87**, 532.

Account of a micrococcus resembling meningococcus and isolated from the purulent cerebrospinal fluid of a boy 8½ years old, who died of meningitis. The microbe differed from meningococcus in being partially Gram +, in its growth on ordinary agar at 22° C., in its failure to ferment dextrose and maltose in recent cultures, in the absence of agglutination with meningococcic serum, and in its relative resistance to deleterious influences. W. B.

Ravaut et **Rabeau.** Sur la virulence du liquide céphalorachidien d'un malade atteint d'herpès génital. [**The virulence of the cerebrospinal fluid of a patient with herpes genitalis.**] *Compt. rend. Soc. de biol.*, 1921, **85**, 1132.

The authors inoculated into the corneae of rabbits the deposit from the cerebrospinal fluid withdrawn from five cases of herpes of the genitals. In one case, the results of the inoculation of which is detailed, the cerebrospinal fluid had an increased cell count and contained albumin. The deposit was inoculated into the cornea without producing keratitis. Fifteen days, however, after inoculation the animal showed nervous symptoms such as turning the head to the side of the inoculation, falling on its side, and jerking of the limbs. Death occurred 28 days later. No macroscopic changes were found at autopsy. Microscopically an examination (by Levaditi) showed

slight irritative changes in the pia mater and prolonged into the septa. In a section including the cerebellum, aqueduct of Sylvius, and mesencephalon lesions typical of human encephalitis lethargica and herpetica were found. At the level of the aqueduct an actual abscess was found with polynuclear cells mostly destroyed. It may be added that the liquid from the vesicles from the herpes case from which the above-mentioned cerebrospinal fluid was obtained was also inoculated into the cornea of a rabbit and produced typical keratitis on the third day and encephalitis on the seventh.

W. B.

Levaditi, C., et **Nicolau, S.** L'immunité dans les ectodermoses neurotropes. [**Immunity in the 'neurotropic ectodermatoses'.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 794.

Levaditi and Nicolau summarize some of the main conclusions to be drawn from their work on the ultramicroscopic virus of herpes and of encephalitis lethargica, as regards their effects on the skin and on other tissues of ectodermic origin (cornea, central nervous system) after injection into one of these tissues, as follows: (1) an animal, which has recovered from a cutaneous or corneal lesion produced by the local inoculation of one of these viruses, is protected against infection if the same virus is subsequently injected into the skin, the brain, or the cornea, with the exception that as between the skin and the cornea the immunity conferred on the one does not extend to the other except on rare occasions and for a very short period; (2) the virus of vaccinia has yielded similar results in their hands, and further experiments are in progress with a view to determine whether the virus of rabies does not belong to the same category of viruses.

The authors therefore class these four diseases together under the term 'neurotropic ectodermatoses'. J. R. P.

Levaditi, C., et **Nicolau, S.** Affinité neurotrope et purification du virus de la vaccine. [**Neurotropic affinity and purification of the virus of vaccinia.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 870.

Levaditi and Nicolau have repeated the experiments of Guérin and Calmette on the results of intracerebral injection of the virus of vaccinia into rabbits. They find that the virus of vaccinia produces in rabbits an encephalitis, which can be reproduced in series for two or three passages only with or without an intervening intratesticular passage, which seems to prolong the number of successful ultracerebral passages.

Recently the authors have succeeded in passing one strain of the virus through a large number of rabbits by simple intracerebral injection. This fixed virus kills a rabbit in 4–6 days. It has preserved its full properties as a vaccine and produces a typical eruption in the rabbit when injected locally or intravenously. Levaditi and Nicolau claim therefore to have turned a purely dermotropic virus into a neurotropic one. J. R. P.

Kling, C., Davide, H., u. **Liljenquist, F.** Den experimentella epidemiska encephaliten hos kanin. [**Experimental epidemic encephalitis in rabbits.**] *Hygica*, 1921, **83**, 705.

These three Swedish investigators note that Levaditi and Harvier have found experimental encephalitis in rabbits to have a short (3 to 10 days)

incubation period, at the end of which the disease usually lasts only a few hours before terminating fatally. Only in a few cases, and after passage of the virus through rabbits, have Kling, Davide, and Liljenquist observed this form of the disease which, in the overwhelming majority of their rabbits, ran a protracted course. In some of their rabbits culture from the brain showed staphylococci, streptococci, and pneumococci in small numbers, but even in these cases of mixed infection, which ran a considerably shorter course than the others, the microscopic changes in the brain were typical of epidemic encephalitis. When the mixed infection was eliminated by various methods, the virus which remained provoked the chronic disease seen in rabbits inoculated with a virus uncontaminated from the onset. And this chronic disease occurred even after five passages through the rabbits of the virus from which mixed infection had been eliminated.

Kling, Davide, and Liljenquist have induced typical epidemic encephalitis in rabbits by the intracerebral injection of filtered (Berkefeld) material obtained from (1) the throat and (2) the stools of patients suffering from epidemic encephalitis. The disease thus induced in rabbits was passed on to other rabbits by intracerebral and intraperitoneal inoculation, five passages in all being effected so far. The rabbit of the third passage died as early as the sixth day after inoculation. This was probably due to exceptional susceptibility of the animal and not to increase of the virulence of the poison, for in the fourth passage the disease returned to a more chronic course. The duration of the disease in most cases was one of several weeks or months, and one rabbit did not die till 7 months after inoculation. But even at an early stage, and during the incubation period, typical changes in the brain were found. Indeed, even when there had been no definite cerebral symptoms, marked changes were observed in the rabbit's brain. It is pointed out that this chronic course of the disease and its sub-latency in the rabbit have their parallels in the human subject, and that Netter is justified in coupling this disease with syphilis in regard to its capacity for lurking more or less unnoticed for a time in the central nervous system. C. L.

Olitzky, P. K. Experimental studies on the etiology of typhus fever. I. Concurrent infections during the course of experimental typhus fever in guinea-pigs. *J. Exper. M.*, 1921, **34**, 525.

The author has studied the occurrence of concurrent infections among guinea-pigs infected with human and louse strains of a Polish typhus fever virus, and of a human strain recovered from a Czecho-Slovak immigrant in New York. The three strains were propagated in guinea-pigs by doses of 3 c.cm. of the blood of other infected guinea-pigs, the bacteria obtainable from blood and spleen at different stages being studied. During the incubation period and before the onset of fever the author found that no ordinary bacteria appeared in cultures, whilst on the first day of the febrile reaction different bacteria occurred in 6 out of 26 guinea-pigs examined; on the second day in 10 out of 16; on the third day in 3 out of 4, and on the fourth day in all of 4 guinea-pigs examined. Apparently the typhus virus predisposes to secondary or concurrent infections with ordinary bacteria, which, however, have no aetiological relation to the specific disease. Among the bacteria cultivated were Plotz's bacillus, *B. welchii*, *Staphylococcus aureus*, *B. proteus*, along with diphtheroids, anaerobic streptococci, and bacilli of Gärtner type. W. B.

BIOCHEMISTRY

McCollum, E. V., Simmonds, N., Shipley, P. G., and **Park, E. A. Studies on experimental rickets. XII. Is there a substance other than fat-soluble A associated with certain fats which plays an important rôle in bone development?** *J. Biol. Chem.*, 1922, **50**, 5.

Hess, A. F., Unger, L. J., and **Pappenheimer, A. M. Experimental rickets in rats. III. The prevention of rickets in rats by exposure to sunlight.** *J. Biol. Chem.*, 1922, **50**, 77.

It seems that we have not yet arrived at complete knowledge upon the rickets question. Previous work by Mellanby in this country, and McCollum and his co-workers, has tended to show that two factors are necessary to prevent rickets, viz. a proper amount of calcium and phosphorus in the diet, and the factor, fat-soluble A. In the absence of a proper amount of calcium, the factor, fat-soluble A, may operate to protect the body to a certain degree against the effects of Ca lack.

(*a*) In the present work McCollum and his co-workers have presented evidence in support of the view that there is, in cod-liver oil especially, another factor, differing from the fat-soluble A. The new factor is held to be especially concerned with bone development and the protection of the body against Ca deficiency. (*b*) The views about the effect of sunlight upon rickets are being placed upon an experimental basis. McCollum and his co-workers have found that sunlight will operate in the same way as cod-liver oil to protect rats against the ill-effects of Ca deficient diet. It must also be remembered that Hess and Unger have claimed that rickets in infants could be cured by short exposures to the sun's rays. In the above paper their work has been extended to rats upon a low phosphorus diet. Such rats regularly develop rachitic lesions in the dark, but do not if exposed for short periods to the light.

The protection may be classed as equivalent to the addition of at least 75 mgm. of phosphorus to the diet in the form of basic potassium phosphate. If the above lines of research are established by future work, it appears that we have an example of the important rôle played by at least one hygienic factor, viz. light, in the prevention of the rachitic condition. This will go some way to clearing up controversy at the present time. The present position may be stated as follows: For the prevention of rickets, enough Ca and P must be present in the diet (in the right proportions, if possible). There is further needed a factor supplied especially by cod-liver oil, which can, to a certain extent, redress dietary errors in Ca and P. Sunlight can apparently supply the place of this last factor. It is most puzzling, from the biochemical point of view, to understand how sunlight can take the place of some organic factor in the diet. R. A. P.

Wright, S. A study of the combined action of raw cow's milk and orange juice as antiscorbutic substances. *Biochem. J.*, 1921, **15**, 695.

When 15–35 c.cm. of raw cow's milk are added to a basal ration already containing 0·5 c.cm. of orange juice, protection from scurvy may be obtained. This figure is considerably less than one would expect if raw cow's milk and orange juice interchanged in proportion to their respective antiscorbutic values. C. G. L. W.

Sheehy, E. J. The origin of milk fat and its relation to the metabolism of phosphorus. *Biochem. J.*, 1921, **15**, 703.

Experiments on cows were performed in which the animals received rations rich in fat or in carbohydrates. Carbohydrates and fat can replace one another in the food for the manufacture of milk fat. It is probable that the substances forming milk fat are phosphatides. These substances in the mammary gland cells are broken up, forming fat and diffusible substances. Among the latter, the diffusible inorganic phosphorus so formed is partly secreted into the milk and partly diffused back into the blood.

C. G. L. W.

Abderhalden, E. Weitere Beiträge zur Kenntnis von organischen Nahrungsstoffen mit spezifischer Wirkung. XI. Versuche an Tauben. XII. Verhalten des Gewichtes und des Wassergehaltes von einzelnen Organen bei Tauben. [**Further contributions to the knowledge of organic food substances with specific actions. XI. Experiments on pigeons. XII. The weight and water content of the individual organs in pigeons.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 329, 355.

XI. Administration of yeast pills to starving pigeons causes an accelerated loss of body-weight; if the yeast is previously heated there is no effect at all. The explanation offered is that the vitamins present in yeast accelerate tissue oxidations.

XII. Most of the organs, but particularly the pancreas and the liver, lose in weight during starvation, and in consequence of avitaminosis induced by a diet of polished rice. The brain, heart, lung, and kidneys, however, retain their normal weight and their normal water content. C. L. E.

Takata, M. Studies in the gastric juice. III. On the empty stomach juice. The secretion at the time when the stomach is empty. *Biochem. J.*, 1922, **1**, 107.

The fasting juice contains pepsine, rennet, nuclease, amylase, and maltase. The amount of mucus secreted in a unit time is not influenced by feeding.

C. G. L. W.

Rose, M. S., and MacLeod, G. Some human digestion experiments with raw white of egg. *J. Biol. Chem.*, 1922, **50**, 83.

Ten healthy young women were given 10–12 raw whites of egg daily. The average co-efficient of digestibility was found to be 80 per cent., only some 6 per cent. less than that of cooked egg white. The absorption occurs rather less readily with raw egg whites than with cooked. It is best when the raw egg whites are beaten lightly. In this connexion Bayliss has shown that raw egg white was digested by trypsin, quite as well as cooked, though at a slower rate. R. A. P.

King, C. E., and Arnold, L. The activities of the intestinal mucosal mechanism. *Am. J. Physiol.*, 1922, **59**, 97.

Microscopic observations of the living intestinal mucosa in the decerebrated dog show, in confirmation of the older work of Brücke and others,

that the villi exhibit shortening, lengthening, and swaying movements. The mucosa as a whole exhibits independent movements due to the muscularis mucosa. The movements of the villi and of the mucosa as a whole are augmented or may be initiated by mechanical stimulation, heat, irritants, and by adrenalin, pilocarpine, atropine, and barium. Cold, anaemia, and shock inhibit the movements. The movements are not subject to vagus control, the splanchnics carry tonic impulses. Meissner's plexus is probably the splanchnic termination. When the outer musculature of the intestine is in tonus, impulses from the mucosa bring about relaxation. This hitherto unrecognized interaction plays probably an important part in determining motor activities of the intestine. W. C.

Meakins, J., and **Harington, C. R. The relation of histamine to intestinal intoxication. I. The presence of histamine in the human intestine.** *J. Pharmacol. & Exper. Therap.*, 1922, **18**, 455.

This research is a contribution to the theory of intestinal intoxication. It is not known to what chemical substances this condition is due, but in view of the great physiological importance of histamine they looked for the presence of this substance in cases of intestinal obstruction. Tests were made by the physiological method of the effect on the uterus of the guinea-pig. Histamine was demonstrated in the caecum and in the transverse colon. Its formation is not dependent upon the existence of intestinal obstruction, since it occurs several weeks after the obstruction has been removed. It could not be detected in the faeces whether there was intestinal disturbance or not. C. G. L. W.

Arai, K. Cholin als Hormon der Darmbewegung. VI. Experimentelle Therapie der Magendarmlähmung nach Peritonitis und Laparotomie. [**Choline as a hormone for intestinal movements. VI. Experimental therapy of gastro-intestinal paralysis following peritonitis and laparotomy.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 359.

According to Magnus and his co-workers choline is the natural hormone for intestinal contractions, and a lowering of the choline production in the intestine, or a lowering of the sensitivity of the intestine to the substance, would result in a condition of stasis. In the present series of experiments, a sero-fibrinous peritonitis was provoked in rats by the intraperitoneal injection of an iodine preparation. Intestinal stasis followed, and was resolved again when 10 mgm. of choline hydrochloride per kilo body-weight was given intravenously. All the findings were controlled by X-ray investigations. Post-operative stasis was induced by performing laparotomy and manipulating the intestines; the results in general were similar to those in the peritonitis experiments. The choline content of the intestine in these experiments was found on analysis to be normal, as was also the response of the isolated intestine to the application of choline. In administering choline it is most important that the intravenous injection be made slowly. Choline borate ('enzytol') may be used, and was found to have a toxicity proportional to its content of choline base. C. L. E.

Kikuchi, M. Beiträge zum Purinstoffwechsel. I. Über das Schicksal des aufgenommenen Purins. [**Purin metabolism. I. The fate of ingested purins.**] *Biochem. Ztschr.*, 1922, **1**, 33.

The amount of total purin compounds excreted in the urine after diets which were known to yield certain amounts of these compounds was determined. The author finds that the amount of purins eliminated in the urine can be calculated from the following formula:

$$Y = (Eo + aX)\ (1 + bX)$$

where X = the purin nuclear nitrogen assimulated, Y is the excreted purin nuclear nitrogen, Eo = the endogenous eliminated purin nuclear nitrogen, a = the kidney co-efficient, and b = the tissue constant. a and b differ in individuals. a appears to be greater in individuals accustomed to a diet low in purins and is especially small in gouty patients. The value of b lies usually between 0·4 and 0·5. As the above formula shows, the amount of excreted purin nitrogen in the same individual is only dependent upon the amount taken in. It does not appear necessary to assume an exogenous fraction and its independence of the change in the condition of the patient.

C. G. L. W.

Staub, H. Untersuchungen über den Zuckerstoffwechsel des Menschen. II. Mitteilung. [**Carbohydrate metabolism in man.**] *Ztschr. f. klin. Med.*, 1922, **93**, 89.

In a further investigation of the effects of 20 gm. of glucose administered fasting on the concentration of sugar in the blood, the author has investigated the effect of fasting. At 10 to 15 hours after the last amount of carbohydrate taken the blood-sugar concentration is at its lowest. With the administration of sugar a slight rise in the blood-sugar curve and a short hyperglycaemia are the signs of good assimilating capacity for carbohydrates. In a good condition of nutrition the diminished tolerance for carbohydrates takes place later than when the subject is under-nourished. This is dependent upon the formation of intermediary ferments during fasting.

C. G. L. W.

Sakaguchi, K., Asakawa, O., u. Matsuyama, T. Über die Bestimmung der Assimilationskraft des Menschen für Kohlenhydrat. [**The estimation of the carbohydrate assimilating power in man.**] *Biochem. Ztschr.*, 1922, **1**, 133.

The estimation of sugar assimilation through an examination of the urine after large doses of sugar is unreliable, because individual normal variations are very great. An investigation of the blood-sugar is of more value, but when this is done after the administration of large doses of glucose the results are not altogether trustworthy. The authors propose a test meal consisting of 100 gm. of dry rice, which is boiled with water, two eggs, and a small amount of vegetable. This is given in the morning instead of breakfast, and the blood-sugar is estimated each half-hour for two hours. When the alimentary hyperglycaemia does not exceed 0·14 per cent., and the blood-sugar level returns to the normal in one to one and a half hours after food, the assimilating power of the patient for carbohydrate is considered normal.

C. G. L. W.

Foster, D. L., and **Moyle, D. M.** **A contribution to the study of the interconversion of carbohydrate and lactic acid in muscle.** *Biochem. J.*, 1921, **15**, 672.

Experiments have been performed to show the reversible transformation of the carbohydrates of frogs' muscle into lactic acid during various conditions of the muscle. The conversion of lactic acid into carbohydrates in the intact muscle is demonstrated, as well as the breakdown of carbohydrates in chopped muscle. The breakdown and synthesis of hexose phosphate in chopped muscle was shown. C. G. L. W.

Dresel, K., u. **Lewy, F. H.** Die Zuckerregulation bei Paralysis agitans-Kranken. [**Sugar regulation in cases of paralysis agitans.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 87.

By administering 25 gm. of glucose it is shown that cases of paralysis agitans react with a hyperglycaemia. Sugar is less quickly assimilated. There is a difficulty in sugar regulation. This is due to a primary disturbance in the vegetative centres of the corpus striatum. C. G. L. W.

Dresel, K., u. **Lewy, F. H.** Die Widalsche Leberfunktionsprüfung bei Paralysis agitans-Kranken. [**Widal's test for hepatic function in paralysis agitans.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 87.

Widal claims that hepatic disturbance can be shown by the fall in the number of leucocytes after a meal consisting of 200 c.cm. of milk administered fasting. The authors found that in paralysis agitans a similar fall takes place. The lymphocytes are especially decreased. C. G. L. W.

HeténYi, G. Untersuchungen über die harnstoffbildende Tätigkeit der Leber bei Leberkranken. [**The urea-forming function of the liver in hepatic disease.**] *Deutsches Arch. f. klin. Med.*, 1922, **138**, 193.

By the administration of a 1–2 per cent. solution of ammonium citrate in amounts corresponding to 4–8 gm. of the salt *per os* the author believes that he can distinguish cases of disturbed liver function. These differ from the normal in that the synthesis of ammonium salts to urea takes 48 to 72 hours, while the normal individual performs a synthesis in 24 hours. The disturbance was most pronounced in cases of atrophic cirrhosis, syphilitic hepatitis, and catarrhal jaundice. It is wise to avoid excessive amounts of protein in these conditions, but a drastic reduction in the diet is unwarranted. C. G. L. W.

Gottschalk, A. Über die Funktion der Leber und Niere in der Schwangerschaft. Ein Beitrag zur Kenntnis des intermediären Kohlenhydratstoffwechsels. [**Renal and hepatic function in pregnancy.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 34.

This is a contribution to the much disputed question as to whether the liver or kidneys are disturbed during pregnancy. The method used was that of Isaac, in which 100 gm. of laevulose in 400 c.cm. of weak tea is administered, and estimation of the blood-sugar and urinary sugar are undertaken at short intervals after administration. In a number of cases of pregnancy no disturbance of the liver or kidneys could be detected. In others, the kidney was permeable to sugar. In a larger proportion of the

cases women in pregnancy showed a distinct insufficiency of the liver, which was manifest by a hyperglycaemia which fell slowly. Urobilin was found in the urine. The excretion of sugar in the urine in normal subjects is dependent on the content in sugar of the renal cells, the amount of sugar in the blood, and especially the length of the hyperglycaemia. The experiments show that the liver and kidneys of the pregnant woman act under certain disabilities, and, for this reason, are liable to damage by toxic substances circulating in the blood during this period. C. G. L. W.

Allen, F. M., and **Wishart, M. B. Experiments on carbohydrate metabolism and diabetes, 4. Dextrose-nitrogen ratios in partially depancreatized dogs.** *J. Metabol. Research*, 1922, **1**, 97.

The ratio of nitrogen to glucose, both in human patients suffering from diabetes and in animals in which the pancreas has been ablated, has been looked upon for many years as a criterion of the severity of the diabetes, and by some it has been thought that a certain ratio indicated a complete loss of function of the cells of the pancreas. The authors show that total excision of the pancreas does not invariably give rise to ' total ' $d:n$ ratio of 2·8 : 1. Diabetes of fatal severity may exist when this ratio is rather low. Microscopic studies confirmed the conclusions of Homans in relating carbohydrate metabolism to the β cells of the islands, but animals which have lost all discoverable β cells may still show a submaximal ratio. On the other hand, no explanation has been found of the rule that where any partially depancreatized animal shows a ' total ' ratio the cells have undergone complete vacuolation or degeneration. The difference between animals which have been partially or totally depancreatized is discussed. Amongst other things it is shown that the power of healing or of resisting infection seems to be almost abolished by total pancreatectomy. C. G. L. W.

Allen, F. M. The pathology of diabetes. I. Hydropic degeneration of the islands of Langerhans after partial pancreatectomy. *J. Metabol. Research*, 1922, **1**, 5.

Portions of the pancreas were removed in dogs and the animals given diets which varied from ordinary mixed diets to fasting. Sections of the organ were cut at various times after the operation. The conclusions reached are as follows :

(1) The hydropic degeneration of the islands of Langerhans is proved to be a specific phenomenon produced solely by overstrain of the function of the cells by diets in excess of the weakened assimilative power. This change is probably reversible within certain limits, and even widely vacuolated cells may probably recover their former size and granulation provided the cell-membrane is not burst or the nucleus become too badly degenerated. The formation of numerous strands and duct-cells and the vacuolation of these and the epithelium of the smaller ducts are described in the end stages of severe diabetes. The demonstration of the nature of the hydropic change is important, for it affords a positive microscopic diagnosis of active diabetes and completes the proof of the island theory of the disease. It affords evidence of the essential identity of experimental and clinical diabetes. It explains the permanent lowering of assimilation in diabetes consequent upon excessive diets and affords the only proved example of anatomical breakdown of cells due to the overstimulation of an internal secretory function.

C. G. L. W.

Martin, W. B. The pathology of diabetes. II. Granule stains of the islands of Langerhans of the diabetic and non-diabetic pancreas. *J. Metabol. Research*, 1922, **1**, 43.

A study was made of the pancreas by special staining methods, using neutral ethyl violet azo-fuchsin or neutral ethyl violet and orange G. The animals used were dogs and cats, and portions of the pancreas were excised at different periods after a first preliminary partial pancreatectomy. They found there are four stages of alteration in the islands of diabetic animals.

(1) The β cells appeared swollen with the falling out of their granular contents.

(2) Vacuolation.

(3) Degeneration.

(4) Disappearance of the β cells, leaving the islands made up of the α cells alone.

The fourth stage has only occasionally been observed in experimental animals and never in a case of human diabetes. It is essential, in order to see these changes, that the tissue be absolutely fresh before fixing.

C. G. L. W.

Allen, F. M. The pathology of diabetes. III. Nervous influences in the etiology of experimental diabetes. *J. Metabol. Research*, 1922, **1**, 53.

No influence of emotion upon the production of diabetes could be demonstrated. Complete separation of a pancreas remnant from its original nerve-supply fails to give rise to diabetes or to any demonstrable lowering of assimilation. The full endocrine potency may be maintained without stimulation or regulation from any special nervous centres. Isolation also fails to affect the occurrence or rate of hydropic degeneration in the strains. This rose parallel with the course of the diabetes the same as when the nerve-supply is left undisturbed. C. G. L. W.

Allen, F. M. The pathology of diabetes. IV. The influence of circulatory alterations upon experimental diabetes. *J. Metabol. Research.*, 1922, **1**, 89.

It has been possible to reduce the arterial supply or venous drainage of pancreas remnants and also to increase the arterial supply to a slight extent. None of these circulatory changes affect the assimilative function or the pancreatic structure. The experiments afforded no support for any circulatory or vasomotor theory of the aetiology of diabetes.

C. G. L. W.

Felsher, H. Curve of sugar excretion in severe diabetes. *J. Biol. Chem.*, 1922, **50**, 121.

Individuals with severe diabetes, who have been brought into the 'sugar-free state' by dieting excrete small quantities of sugar, 10–15 mgm. per kilo per day, not differing much from the normal individual. As the diet is increased at 1–4 day intervals, there comes a sudden critical point at which the sugar elimination shows a rapid acceleration. R. A. P.

MacKinlay, C. A. Effect of extract of posterior lobe of pituitary on basal metabolism in normal individuals, and in those with endocrine disturbances. *Arch. Int. Med.*, 1921, **28**, 703.

The subcutaneous injection of the extract produces a rise in the basal metabolism of normals, the rise being more marked if an injection of thyroxin has been given beforehand. In a few cases of hypothyroidism the basal metabolism was diminished rather than increased. In four cases of subnormal basal metabolism, without clinical evidence of myxoedema, the normal response to pituitary extract was present. O. L. V. de W.

Johannessen, A. Om kvalitativ og kvantitativ Paavisning af Blod i Urin. [**Qualitative and quantitative demonstration of blood in the urine.**] *Ugesk. f. Læger.*, 1921, **83**, 1613.

Johannessen first discusses the many shortcomings of the guaiacol test for blood in the urine, and then describes comparative investigations made by himself into the benzidin, fluorescein, and phenolphthalein tests, the last of which he has found the most simple and delicate. He uses the same solution as Boas does for examining the faeces for blood, the formula being: phenolphthalein gm. 1, potassium hydroxide gm. 25, distilled water gm. 100. This solution is boiled with 10 gm. of zinc dust to decolorize it. Then it is filtered. An equal quantity of 96 per cent. alcohol is added to the solution, and to each 9 c.cm. of this mixture 1 c.cm. of hydrogen peroxide is added. To 0·5 c.cm. of this reagent in a small test-tube 0·5 c.cm. of the urine to be tested is added; if it contains blood, a red colour appears, varying from pink to carmine red according to the amount of blood present. Johannessen has worked out a scheme of quantitative analysis, using a fixed quantity of the phenolphthalein solution to which only one drop of the urine is added. If a positive reaction is obtained, the urine is diluted with distilled water, the dilution being proceeded with step by step till one drop no longer gives a positive reaction. He found that the phenolphthalein solution to which hydrogen peroxide had been added would keep its original properties for 10 to 14 days, and that when hydrogen peroxide was not added till the last moment to the alcoholic solution, this would keep for at least half a year. Accordingly, he recommends the addition of hydrogen peroxide to the stock solution only just before use.

Johannessen has worked with this test for more than a year and has found that a positive reaction can be obtained with blood in water in as high a dilution as 1 in 500,000, i. e. 10 red cells per c.cm. In the presence of urine the test is less delicate as the salts of the urine interfere with it; but is positive in as high a dilution as 1 in 20,000–30,000, i. e. 150–250 red cells per c.cm., the differences depending on the concentration of salts in the urine. The test was positive when 1/20–1/30 c.cm. of blood was added to 1 litre of water. The test can be made still more delicate by examining only the sediment of urine which contains blood. Johannessen has found the test strictly specific with the one exception that copper salts give a positive reaction; test-tubes that have been used for examining for sugar should, therefore, not be used. Otherwise, he has never obtained a positive reaction without also finding blood by microscopic examination. Pus gave a negative reaction, as did a host of drugs such as camphor, digitalis, strophanthus, codein, morphine, potassium iodide, salicyl, decoct. chinae, iron, arsenic, mercury, diuretin, salol, thyreoidin, sodium bicarbonate, castor oil,

and cascara. Charts are published, showing how the varying severity of haematuria in a given case may be registered by the quantitative test. And the suggestion is made that this quantitative test may prove of as great prognostic value as the quantitative tests for albumin in the urine.

C. L

Klein, O. Über den Reststickstoffgehalt des Blutes bei arteriosklerotischen Hypertonien, ein Beitrag zur Kenntniss der Nierenfunktion bei den benignen Nierensklerosen. [B.] [**Rest nitrogen in the blood in hypertonic arteriosclerosis and renal function in benign sclerosis of the kidney.**] *Deutsches Arch. f. klin. Med.*, 1921, **138**, 2.

The renal function in relation to arteriosclerosis was examined in 54 cases in an attempt to discriminate between the views of Fr. Müller and others, who look upon the permanently high blood-pressure as a result of the permanent affection of all the small arteries of the greater circulation, and those of Romberg, who believes that the rise in pressure is due to the same causes as that of nephritis, viz. a change in kidney circulatory function. There are some observers who take a middle course.

The experiments correlated the blood-pressure in the cases examined with rest nitrogen determinations in the blood. Certain concentration tests were undertaken by giving the patients a known amount of water and determining the time taken for its excretion. Benign sclerosis of the kidney is marked by great variation in the concentration of rest nitrogen in the blood at different times. This differs from what is observed in renal conditions of a more serious character. Other clinical symptoms have a similar 'labile' form. The compensatory relation of heart and kidney is emphasized, and it is shown that there is no real boundary between a benign and more serious condition of the kidneys. The main point of difference between the two is that in the former the manifestations are periodic or transitory ; in the latter, constant. The periodic type is not due to cardiac stasis for there is no evidence of general insufficiency of the heart. The rise in blood-pressure and blood nitrogen must be put down to an increase in the resistance of the kidney to the blood-flow, due to a functional contraction of the renal arterioles. C. G. L. W.

Rohonyi, H. Ueber die Säureausscheidung bei Nierenkrankheiten. [**Acid excretion in renal disease.**] *Ztschr. f. klin. Med.*, 1921, **91**, 105.

The author has investigated the ratio of acid and basic phosphates in the urines of nephritic patients. This was done by titrating samples of the urine with acid, using alizarin red, and with alkali and phenolphthalein respectively. By the former he estimated the amount of dibasic sodium phosphate, by the second the amount of monobasic phosphate. He draws his conclusions from the ratio of the acid over the alkali phosphate.

In the morning urine (12 hours after food) the amount of acid salts is greater than the alkaline in normal cases. The reverse is the case with certain renal cases in which the tubular epithelium is affected. These cases, secreting an alkaline fasting urine, are quite capable of secreting acid salts, provided these reach the kidney. The ammonia quotient in these cases is not high. It is suggested that the alkalinity of the urine is of extra-renal origin. C. G. L. W.

Ehrenberg, R., u. Karsten, A. Harneisen und Nierenfunktion. [**Urinary iron and kidney function.**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 86.

The authors regard urinary iron as a product of the metabolic activity of the kidney itself. The daily amount of about 1 mgm. of iron, which is chiefly in organic combination, is unaffected by the intake of iron per day, but varies, as a rule, inversely as the volume of urine passed in the day. That is to say, the greater the work done by the kidney in concentration, the greater the amount of iron passed in the urine. In diuresis, there is, however, also an increase in the amount of iron passed. C. L. E.

Priestley, J. G. Regulation of excretion of water by the kidneys. *J. Physiol.*, 1921, **55**, 320.

Ingestion of large amounts of water, while producing great diuresis, leads to no change in the haemoglobin content of the blood, but is accompanied by a slight fall in the electrical conductivity and chloride content of the blood. The water absorbed is only taken up by the blood to a small extent, the remainder being stored in the tissues, with chlorides and possibly protein which has passed out of the blood. Great increase in diuresis after water is accompanied by a transitory increase in the total chlorides excreted per hour, but if the chloride content of the body is depleted this rise in chloride excretion does not accompany the diuresis. Pituitrin delays the onset of the diuresis by 4 to 6 hours, but since the same blood changes occur, and no diarrhoea results, it is suggested that the action of pituitrin is on the kidney cells, and that the effect produced is not due to interference with absorption. O. L. V. de W.

Becles, C., and **Fitz, R. Observations on glycaemia, glycuresis, and water excretion in obesity.** *Arch. Int. Med.*, 1921, **28**, 804.

The authors investigated 32 obese patients, the glucose tolerance being estimated by the method of Hamman and Hirschman (blood-sugar by Folin and Wu's method), and quantitative estimations of the urinary sugar being made by the method of Benedict and Osterberg. A dose of 100 gm. of glucose was employed. In 8 cases a hyperglycaemic type of curve was obtained; in the remainder the blood-sugar curve was approximately normal. In many instances a smaller amount of sugar was excreted, during the test, than in normal individuals. They suggest that in these cases sugar is utilized or stored with abnormal rapidity. In the cases showing a hyperglycaemic curve, an increased glycuresis is found, and clinically these cases are to be regarded as early diabetics. The dose of glucose could not, however, be graduated according to body-weight, since the large doses required in the obese produce nausea and vomiting. O. L. V. de W.

Witzemann, E. J. The catalytic effect of ammonia on the oxidation of butyric acid with hydrogen peroxide. *J. Biol. Chem.*, 1921, **49**, 123.

Shaffer, P. A. Antiketogenesis. III. Calculation of the ketogenic balance from the respiratory quotients. *J. Biol. Chem.*, 1921, **49**, 143.

These two papers are suggestive in connexion with carbohydrate metabolism.

In the presence of ammonia and potassium, hydrogen peroxide will oxidize butyric acid to acetone and carbon dioxide. This observation was

made some time ago by Dakin, but it has been extended here in several respects. The presence of potassium has been shown to be essential. It has also been found that the effect is best produced when there is one equivalent of each of the bases present. Sodium will take the place of potassium, though there is a slight difference in the result. It is held to be established that the effect is specific and not due to alkalinity. If these results are put into relation with the fact that Embden and Kalberlah showed that the liver formed aceto-acetic acid, and that the liver is normally concerned in the transformation of ammonia bodies into urea, they are certainly suggestive.

In a previous paper, Shaffer showed that the oxidation of glucose by hydrogen peroxide in alkaline solution brought about the rapid disappearance of aceto-acetic acid if the latter was present. This was held to be an *in vitro* analogy to the known effect of carbohydrate in preventing the appearance of acetone bodies in the urine. Upon a basis of this nature, an attempt was made to calculate the ratio of ketogenic to antiketogenic bodies present in several well-known experiments in the literature. The assumptions were made that each molecule of fat was convertible into (*a*) 3 mols of aceto-acetic acid and (*b*) 0·5 mol of glucose, or its equivalent antiketogenic derivative, and further that protein was convertible (*a*) into antiketogenic glucose or its equivalent to the extent of 3·6 gm. for each gm. of urine N, and (*b*) into aceto-acetic acid for each mol of leucine, phenylalanine and tyrosine; (*c*) the amino-acids—valine, lysine, histidine, and tryptophane—are neutral as to ketogenesis. Further, carbohydrate exerts its antiketogenic action in the form of glucose or other hexose, 1 gm. being equivalent to each 5·56 millemols of antiketogenic substance.

Upon this basis it appeared that acetone bodies first appeared when the mol ratio of ketogenic to antiketogenic bodies exceeded 1 : 1. In this paper an examination of the data culled from the literature upon the respiratory quotient shows that the critical ratio is at the point of 0·76. This is said to correspond with a mol ratio of 1 : 1. Below this there is excretion of acetone bodies. R. A. P.

Fischer, R. Zur Pharmakologie des Kohlenoxysulfids. [**On the pharmacology of carboxysulphide.**] *Biochem. Ztschr.*, 1921, **125**, 12.

Carboxysulphide (COS) has in certain early work been considered as the cause of malaria. It is shown by the author that the symptoms of poisoning are mainly those of H_2S, owing to the rapid destruction of the COS. Where death occurs in animals, it is due to respiratory failure. Frogs are much less sensitive than rabbits. A concentration of 0·49 per cent. for one hour killed rabbits in two days. 0·24 per cent. for 65 mins. produced effects upon the central nervous system. No blood change was observed in the animals poisoned with COS, though *in vitro* COS forms sulph-haemoglobin. R. A. P.

Widmark, E., und **Jeppson, C. H.** Ein definierter organischer Katalysator mit Wasserstoffionen-optimum. [**A definite organic catalyst with hydrogen-ion optimum.**] *Skandin. Arch. f. Physiol.*, 1922, **42**, 43.

It is known that the decomposition of aceto-acetic acid into acetone and carbonic acid proceeds more rapidly in the presence of organ-extracts and

blood serum. It was found further that this action is not due to a ferment but to the presence of definite organic substances present in the mixture and that it depends on the presence of an amido group in these organic substances. The authors have studied the action of one of these substances, anilin, which acts as a catalyst, on the decomposition of aceto-acetic acid. They find that the catalytic action of aniline is dependent on a certain optimum concentration of hydrogen ions. The interest of these observations lies in the fact that most ferments are also dependent for their action on a definite hydrogen-ion concentration. The present case is the first example of a simple organic substance behaving in this respect like a ferment.

W. C.

Abderhalden, E., u. **Gellhorn, E.** Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung. VI. [**Further studies on the substances with specific actions elaborated in certain organs.**] *Arch. f. d. ges. Physiol.*, 1921, **193**, 47.

The name S-optones is given to the class of products obtained by hydrolysis of organs with 10 per cent. sulphuric acid; N-optones are obtained by hydrolysis with proteolytic enzymes; the extract called C is the extract obtained by removal of all alcohol-soluble components. Testis optone S has a stimulating action on the isolated heart, while the testis N has not this effect; the effect is, however, unmasked by acid hydrolysis of N, and is even more marked in C. Placenta N first retards and then increases the heart-beat, while S simply depresses and retards it. Thyroid and goitre hydrolysates, and testis C cause contraction of plain muscle (frog's oesophagus). Placenta S in dilute solution also causes contraction, but N, and S, if concentrated, produce relaxation. Thyroid, pituitary, thymus, ovary, placenta N, and testis S-optones all cause intense capillary dilatation, as judged by microscopical observations on the frog's web, and can overcome the constricting effect of adrenalin. It is suggested that the endocrine organs may, by production of such substances, play a part in the regulation of capillary tone. (The authors seem to forget that these hydrolysates only remotely, if at all, resemble the intact tissue chemically, and still less, in all probability, its active secretion.) C. L. E.

Weinberg, M. H., and **Schubb, T. Experiment in a new method of therapy of paralysis agitans.** *Proc. Soc. Exper. Biol. & Med.*, 1921, **19**, 21.

Starting out from the premise that paralysis agitans is due to hyperparathyroidaemia, the authors removed the two external parathyroids from a goat. Forty days after, blood was withdrawn and administered to Parkinsonian patients. Promising results seem to have been obtained.

C. G. L. W.

Rettger, L. F., and **Cheplin, H. A. Therapeutic application of bacillus acidophilus.** *Proc. Soc. exper. Biol. & Med.*, 1922, **19**, 72.

The authors report a series of 29 cases, 20 of which were chronic constipation, the others being chronic diarrhoea, colitis, sprue, and eczema. These were treated with either milk implanted with *B. acidophilus* or lactose and whey cultures of the organism.

In every instance of chronic constipation the treatment was sufficiently successful to allow the patients to dispense with the use of cathartics. The

history of the other patients showed with some exceptions a distinct improvement in condition after treatment which (in the cases cited) did not exceed three months. C. G. L. W.

Maxwell, S. S., Burke, U. L., and **Reston, C. The effect of repeated rotation on the duration of after-nystagmus in the rabbit.** *Am. J. Physiol.*, 1922, **58**, 432.

Daily rotation reduces in the rabbit the after-nystagmus. This is more pronounced when the head is left free during rotation than when the head is fixed. The rotation was in the plane of the horizontal canals. The caloric test gave no evidence that the labyrinth had been injured by the amount and rate of rotation, and the conclusion is arrived at that the animals have become less responsive through habituation. W. C.

RADIOLOGY

Radiotechnique

Dessauer, F., u. **Vierheller, F.** Die Tiefenwirkung der Röntgenstrahlen. [**The deep effects of X-rays.**] *Strahlentherapie*, 1921, **12**, 655.

The paper contains the results of an elaborate series of measurements upon the intensity of the radiation at different depths in the tissues when subjected to X-rays applied externally.

The problem is a highly technical one, and the authors give the methods they employ, not only for finding the intensity at different depths in the tissues, but also how the variation in this intensity may be reduced by selecting different ports of entry for the primary beam. The difficulty of administering a uniform dose of radiation to a mass of tissue at a depth below the surface is a very real one, and moreover one which is not likely to be overcome without physical measurements of an elaborate character. The authors work over a wide range of spark-gap, and utilize rays which have been filtered by various metals. Generally speaking, the shorter the wave-length of the radiation at one's command the simpler becomes the technique of administering a uniform dose of rays throughout a mass of tissue; this, in the main, is the justification for the use and indeed the demand for apparatus which is capable of producing X-rays of appreciably shorter wave-length than is usually at the command of the radiologist. S. R.

Radiotherapy.

Haret et **Truchot.** Quelques résultats de l'emploi des hautes doses avec rayonnement pénétrant en rœntgenthérapie profonde. [**Some results from using heavy doses of penetrating rays in deep X-ray therapy.**] *J. de radiol. et d'électrol.*, 1921, **5**, 486.

The authors describe a case of lymphadenoma that came to them for treatment, in the course of which they were led to believe that heavy doses

were of much greater use than small ones. Since July 1920 they have used heavy doses up to 30 H units by each port of entry. Fifteen cases of various types have been treated by the authors with only one failure; a *résumé* of the treatment is given, and the paper closes with notes on all 15 cases. They believe that all neoplasms should be treated on these lines, which are not dangerous if the technique be good. P. L.-B.

Quick, D. (1). **Pre-operative and post-operative X-ray in carcinoma of the breast.** [**B.**] *Am. J. Roentgenol.*, 1920, **7**, 597.

Quick, D. (2). **The combination of radium and the X-ray in certain types of carcinoma of the breast.** [**B.**] *Surg. Gyn. & Obstet.*, 1921, February, 156.

The author expresses the hope that the number of cases in which X-rays are applied both before and after operation will increase: surgery alone, in his opinion, leaves room for much help from other agents. Various authors favouring post-operative X-rays are quoted. The author does not agree that the production of a premature menopause helps to check metastases. Stress is laid on the fact that some authors state that X-rays alone can apparently check the appearance of metastases. The advantages of pre-operative irradiation are mentioned, and details of a case in which X-rays were applied both before and after operation are given. For over two years the author has treated every case of primary breast cancer by pre-operative X-rays, and in doubtful cases the question of subsequent surgical intervention is put off for two to four weeks. The technique of irradiation is described in detail; daily treatment is given, the number of exposures depending on how the patient stands the treatment; usually two to four areas are irradiated at a sitting. The further treatment of cases is described; strictly operable cases are operated upon a fortnight later, so that the skin is in a condition to stand post-operative irradiation as soon as the patient is out of bed again. The routine post-operative treatment is to give each patient three complete cycles at intervals of a month, following essentially the lines of pre-operative treatment but not so rapidly; four to six months after the third cycle a fourth is given as an added precaution.

The author states that X-rays now occupy a place in the treatment of every case of carcinoma of the breast, and various authorities are quoted. This is followed by a review of the literature on the use of radium in this type of case. It is pointed out that in using radium accuracy and intimacy of application are essential to a good result. References are made to cases in which radium was buried in the growth and it is noted that the less the filtration the better the result, but the author points out that in no case were sufficient tubes used to produce uniform radiation through the tumour. The uses of X-rays and radium are compared and contrasted.

For the past two years the author has tried to combine the two agents. The method by which prolonged radiation is applied by means of buried tubes of radium emanation is described; nearly all the beta rays are used and the author considers that this is probably the most important feature of the method: this is followed by a description of the X-ray treatment, which is as thorough as if no radium had been applied. Twelve cases are reported with the histories and treatment applied on the above-mentioned lines, and the author claims that the results are an advance in treatment. Seventy-eight cases have been treated on these lines, 57 being recurrent or metastatic

tumours and 21 primary; the results of treatment are given. As the cases which call for physical treatment alone are usually the worst cases, the author points out that in the main treatment can only be palliative. The types of case in which radium is of value in conjunction with X-rays are tabulated. It is claimed that the treatment is based on sound theory as it intensifies the natural reaction of the tissues to carcinoma, and at the same time produces a very strong destructive action on the tumour-cells.

P. L.-B.

Nogier, T. Radiodermite grave de la paroi abdominale au cours d'un traitement de fibrome utérin malgré l'emploi de doses faibles et de rayons X filtrés sur 3 et 4 millimètres d'aluminium. Grossesse ultérieure. [**Severe radiodermatitis of the abdominal wall during treatment of a uterine fibroid in spite of using weak doses and X-rays filtered with 3 and 4 mm. of aluminium. Subsequent pregnancy.**] *Arch. d'électric. méd.*, 1921, **29**, 299.

The article consists of the complete record of a case in which a woman consulted the author about a uterine fibroid on November 11, 1912, and was treated until September 16, 1913, after which various complications arose; these are enumerated in full. The object of the article is to point out that even weak doses with much screening can bring about serious effects on the abdominal wall. The ovaries were not destroyed, since menstruation recommenced 17 months after the last séance, and about three years later the patient became pregnant.

The cause of the dermatitis, according to the author, must have been due to an accumulation of the doses. To avoid similar accidents one must (*a*) carefully localize the pencil of rays applied; a field 8 cm. in diameter appears to the author to be the maximum for each part; (*b*) avoid irradiating the middle line of the abdomen; (*c*) avoid overlapping the fields irradiated; (*d*) use a thicker filter than 4 mm. of aluminium for deep lesions; (*e*) the distance from the anticathode to the skin should be at least 30 mm.[1] [*sic*]. If menorrhagia reappears or the fibroid enlarges, the only treatment is intra-uterine applications of radium. As regards the question as to whether radiotherapy radically suppresses the ovarian function, the author believes that his case shows that it may not since a dose of 40 H units failed to do so in a young woman.

The following is a *résumé* of the treatment:

Time Since Previous Séance.	Region Irradiated.	Filter.	Distance of Anticathode from Skin.	Duration in Minutes.	Dose in H Units Measured on the Skin.
—	The whole abdomen (compression)	3 mm.	240 mm.	40	4·75
28 days	,, ,,	3 ,,	260 ,,	40	5·25
35 ,,	,, ,,	3 ,,	260 ,,	40	6·5
42 ,,	,, ,,	4 ,,	260 ,,	40	4·75
34 ,,	,, ,,	4 ,,	240 ,,	35	4·0
50 ,,	Fibroid with Drault's localization 8 cm. in diameter	3 ,,	270 ,,	30	4·75
42 ,,	,, ,,	3 ,,	220 ,,	30	4·75
78 ,,	,, ,,	3 ,,	225 ,,	35	4·5

[1] Presumably this is a misprint for 30 cm. judging from the table.

P. L.-B.

Quick, D. Treatment of carcinoma of the tongue. [B.] *Ann. of Surg. Phila.*, 1921, June, 716.

The author states that this is one of the most difficult types of carcinoma with which to deal, and that it is very fatal. Surgery alone has proved inadequate and unsatisfactory. In the author's series only 27 per cent. were operable at the time of applying for treatment; other limitations to surgery are mentioned. A review of statistics of various authorities is given.

Treatment of the primary lesion. According to the author this part of the disease belongs entirely to the field of radium. Surface application is only used in a very limited number of cases, buried emanation tubes supplemented by surface application being the rule. Tubes containing one millicurie or slightly less have been found to give the best results. The method of inserting the tubes is described. The most important factors are uniformity of distribution and accuracy of approximation throughout the growth. The differences and advantages between this method and burying the element in metal containers is discussed. By this method the treatment is both prolonged and intense, and is not painless, so that the patient must be continually encouraged. The mouth must be kept scrupulously clean, and the physical condition must be kept up.

Treatment of the cervical nodes. In this the author takes up a very conservative position: recently external radiation has been applied in all favourable cases. The glands are looked upon as protective organs, and in the author's opinion should not be interfered with surgically unless they are definitely involved in the disease. The technique of treating an early palpable gland is described. Operations are carried out under local anaesthesia, a point on which the author lays great stress.

Statistics of the 148 cases treated during the last $3\frac{1}{2}$ years are given in full. P. L.-B.

Radium Therapy.

Edling, L. On plastic means of application in radium therapy. [B.] *Acta Radiol.*, 1921, **1**, 60 and 219.

The author points out that the technique of application has not kept pace with the development of methods of dose and filtering. The characteristics of an ideal method of application are enumerated, and the five main methods at present used are described and discussed, none of which even approximately fulfils the conditions of the ideal method.

A. **General part.** 1. *Origin and development of the plastic method.* This originated in 1910 in connexion with a case of sarcoma of the tonsil, but nothing was done for five years, when Trilbis' dental composition was used. The method as gradually developed is explained, and the uses of plastic substances in other countries is referred to shortly. 2. *Chemical and physical analysis.* The physical properties necessary are enumerated; of the substances examined, Kerr's alone is suitable; this contains 50 per cent. of inorganic material, which is an important factor from the point of view of secondary filters. Experiments were carried out on the following lines: (*a*) measurements of the absorption of the primary radiation of the radium by the different secondary filters; (*b*) measurement of the emergence radia-

tion of the different secondary filters; (*c*) measurements of the emergence radiation of combinations of lead filters and various secondary filters. Graphs illustrating these measurements are given. 3. *General principles for the use of the plastic method of application in radium therapeutics.* The method of preparing the plastic substance is described; hairy parts should be shaved, and in all cases the skin greased to prevent sticking, this also applies to the operator's fingers. The preparation of the applicator and the insertion of the radium tubes is described at some length. It is estimated that an applicator costs from 1 to 2 shillings, and if made of Kerr's substance can be used more than once; the method of sterilizing is described.

B. **Special part.** This deals with the use of the plastic method for tumours in various parts of the body. 4. *Tumours of the face, head, and external regions.* In most cases the applicator must surround the tumour for some distance: if there be painful ulceration the surface of the ulcer should be covered by a thin compress of ointment. Illustrations of various cases are given to demonstrate the method. In cases of tumours of the concha of the ear, it is advisable to carry out the treatment at one sitting. The technique of making an applicator for non-prominent or flat tumours is described. It is asserted that the method can be used in widely separated surfaces of the skin. 5. *Tumours of the eye-lids, canthi, and orbits.* In these cases the method is claimed to be far superior to any older methods. The eyeball must be well protected from irradiation and mechanical irritation. The technique for the various types of cases is described. 6. *Tumours of the lips and the cavity of the mouth.* The difficulties of irradiation in this area are pointed out, especially the very painful radium dermatitis which may occur. Two methods of treating carcinoma of the lip are described and illustrated: it is pointed out that a recurrence after operation is usually difficult to treat on account of cicatrices. Radium treatment is preferred to surgical because of the better cosmetic and functional results. The treatment of angiomata of the lip is described with the technique. The author states that the treatment of buccal tumours is much more difficult owing to the more limited space; two methods are described. The results of treating these tumours has led the author to the conclusion that they are not very suitable for radium treatment, especially if they have begun to infiltrate. As regards tumours of the jaws and hard palate, it is asserted that the plastic method removes the former difficulties: the method is described, including that for cases which have had resection of the upper jaw. The tendency to necrosis in these cases is mentioned, also the great need for adequate filters in all mouth cases. The methods for treating tumours in various parts of the tongue are also dealt with, and it is stated that the prognosis is relatively good if only large doses are used concentrated within a comparatively short time. To prevent thirst a glass tube can be inserted in the applicator, through which water may be sucked, and the lips smeared with vaseline to prevent dryness. 7. *Tumours in the upper air passages (including the palatine arches and tonsils).* As regards the back and upper parts of the nasal cavity, fixation of the tubes by tamponade or the introduction by means of a catheter are recommended: for the front part of the nasal cavity the plastic method can be employed. As regards tumours of the maxillary antrum, resection of the upper jaw is advised, but where this is impossible the method of using the plastic substance is described. Treatment of tumours of the nasopharynx is dealt with at some length. Tonsillar tumours are also dealt with at length and the method fully illustrated, as

they are only treated with difficulty. 8. *Tumours of the penis.* The necessity of absolute protection for the scrotum is mentioned, and the author claims that the plastic method does away with the old difficulties. The mode of application is explained. 9. *Rectal tumours.* Dilatation of the sphincter is recommended and also a previous colotomy. By means of the plastic method it is claimed to be comparatively easy to ensure an exact and certain application of radium and filters. The method of application to discoid and circular growths is given. As regards tumours situated in the immediate vicinity of the sphincter, the author inclines to restricting radium as far as possible and using deep rays for reasons which he states. 10. *Tumours in the female genitalia.* For intra-uterine and intracervical tumours the plastic substance is unsuitable. The methods of application to various situations is described, some at length with five illustrations. As regards gynaecological cases, the author states that the branch that has derived greatest benefit from the plastic method is the treatment of vulvar carcinoma.

P. L.-B.

Bailey, H., and **Quimby, Edith. The use of radium in cancer of the female generative organs.** *Am. J. Obstet. & Gynec.*, 1922, **3**, 117.

Technique for cancer of the cervix. The authors' work began in 1915, at which time 50 mgm. was the largest quantity of radium obtainable. The chief factor was the intracervical application of radium filtered with 2 mm. of lead and a vaginal application. Cross-fire was also employed. Under these conditions 10 per cent. of the cases treated are still free from the disease, but owing to many patients developing a recto-vaginal fistula the technique had to be changed. By this time 100 millicuries of emanation was used, three applications within the cervix and the neck of the uterus being employed with 1 mm. platinum screen. The vagina was packed with gauze so as to push the bladder and rectum as far from the cervix as possible. During 1915–16 a Percy operation was performed in 30 cases and radium applied later, but the results were not good, probably due to an interference with the blood-supply of the parts. Later, the papillomatous parts of the lesion were burnt away from below without opening the abdomen. The authors then go on to describe the development of the 'bomb' technique, by means of which doses of 3,000 millicurie hours have been given with little effect on the bladder or rectum. Three radiographs illustrate the method. The block treatment, by which patients received from 9,000 to 18,000 millicurie hours, is then described and illustrated. Since 1919 the embedding of glass tubes containing emanation has been used more and more, particularly in vulvar and vaginal carcinomata. The measurement of radiation is gone into at length. The unit of radiation selected was the 'skin dose', and corresponds to 3,200 mc. hours with a filter of 0·5 mm. of silver, 2 mm. of brass, and 1 cm. of bakelite in a brass applicator, the radium being 4 cm. from the skin.

Cancer of the body. The technique depended upon whether the uterus was to be removed after treatment or not; the authors believe this should be done in all cases where practicable. The dose is 3,500 mc. hours within the body of the uterus and hysterectomy is performed after 6–8 weeks, followed by external radiation by the block technique. If the uterus is not to be removed the same internal dose is given supplemented by both bomb and block methods.

Cancer of the vagina and vulva. Buried emanation is used, each tube containing about 0·5 mc., supplemented by both block and bomb technique. In cases of recurrent cervical carcinoma this method is also used.

A discussion of the results for 1915–20 follows, during which period 600 cases of uterine carcinoma and 32 cases of vaginal and vulvar carcinoma were treated and the cases followed up. The authors feel that the technique has been standardized since 1918, and that better results should follow. Each type of case is then discussed under its appropriate heading. In conclusion, the danger of over-irradiating the tissues in prophylactic treatment after hysterectomy is pointed out. P. L.-B.

Radiobiology

Lacassagne, A., et **Monod, O.** Les caryocinèses atypiques provoquées dans les cellules cancéreuses par les rayons X et γ et leur rôle dans la régression des tumeurs malignes irradiées. [**Atypical karyokinesis induced in cancer cells by X-rays and γ-rays and their rôle in the regression of irradiated malignant tumours.**] [**B**]. *Arch. franç. de Path. gén. et expér. et d'Anat. path.*, 1922, **1**, 1.

In order to study the cytological action of radiations on malignant cells the authors carried out the following experiments:

The disappearance of malignant tissue in a sarcoma in a bitch. A. The animal was received at the laboratory on February 11, 1921: there was a large tumour in the right mammary region. It was proposed to remove the tumour and carry out autografting; this was done the following day, but the tumour was not completely removed. On February 28 the site of the original tumour was ulcerated and the four autografts were positive. The animal was then irradiated, receiving 20·5 H units over 5 hours 20 minutes. Portions of the tumour were removed for examination on eleven occasions from 21 hours after irradiation to March 14, in each case from the right edge of the tumour. A short description of the wound from March 2–14 is given; on the latter date it is described as characteristic. On March 26 the animal was killed. *B.* The method of embedding the specimens and staining the sections is described, and the various types of abnormal karyokinesis are enumerated, and their histological appearances described. This is followed by a description in detail of the examinations of sections removed on the above-mentioned occasions. The following cytological phenomena followed irradiation during regression of the tumour: (1) during irradiation disappearance of cellular division and suspension of all new mitoses; (2) during the first few hours after irradiation re-establishment of mitoses, which 18 hours later are as numerous as before irradiation, but anomalies are frequent; (3) from the 3rd–5th days inclusive the following phenomena became more and more marked: (*a*) disappearance of the most superficial layers of the ulcerated tumour; (*b*) the appearance of considerable reparative activity; (*c*) more and more marked anomalies in mitosis; (*d*) in spite of the active cell-division a rapid reduction in the neoplastic cells; (*e*) atypical cell-division leads to a certain number of giant cells; (4) after the 5th day, cessation of mitosis in some of the remaining giant cells, most of which are disintegrating; (5) after the 7th day disappearance of all the malignant elements.

The disappearance of malignant tissue in human tumours. The results of examinations made from tissue removed during and after X-ray treatment in the case of human malignant tumours have shown several of the cytological phenomena similar to the above, and the authors state that, as a general rule, the process of regression by degenerative mitoses as described for a sarcoma in a dog holds good in many cases of human cancer, particularly in squamous-cell carcinoma. Short notes are given on five cases treated by radium, in which a series of examinations was made, four being cancer of the neck of the uterus and one cancer of the face. These observations show that certain phenomena are constant, and these are very approximately the same as those found in the dogs. Stress is laid on the following points: Irradiation causes an almost immediate disappearance of the existing karyokineses, there is no latent period before the rays exert an effect. This phase lasts several hours, and is followed by greater and greater cell activity; this is 'degenerative mitosis'.

The authors complete their paper by a lengthy synopsis of the literature on the subject, from which they conclude that their observations are not new, but that their value has not hitherto been fully appreciated. P. L.-B.

McQuarrie, I., and **Whipple, G. H. A study of the renal function in Roentgen-ray intoxication. Resistance of renal epithelium to direct radiation.** [**B.**] *J. Exper. M.*, 1922, **35**, 225.

The authors refer to an earlier paper in which they recorded a transient disturbance in renal function in the intoxication due to intestinal obstruction. Following the work of Hall and Whipple, who pointed out the clinical similarity between intestinal obstruction and systemic X-ray intoxication, they studied the renal function in X-ray intoxication. Their results show that the renal function is uninvolved under the latter conditions, and the absence of anatomical evidence of cell injury: they conclude that the renal epithelium is much more resistant to X-rays than is that of the small intestine. A short summary of the findings of other workers is given. The technique is described at length; in all cases normal adult dogs were used, and in most cases a 9-inch spark gap with about 90 kilovolts and a distance of 25 cm. from the anticathode to the surface of the body were used. The ammeter in most cases read 8 milliamps, but in a few cases varied from 5–10 milliamps. The experiments were carried out on three lines: (i) sub-lethal doses given at intervals over relatively long periods; (ii) a lethal dose given over the abdomen with the kidneys and remainder of the body screened from direct rays; (iii) the kidneys were exposed directly to huge doses of X-rays, while the remainder of the abdomen and the thorax were shielded. The various sets of experiments are illustrated by tables and short notes on individual dogs, with post-mortem findings.

The experiments lead the authors to the conclusion that the usual therapeutic doses of X-rays can be given over the kidneys without any fear of causing any damage. P. L.-B.

Mottram, J. C., and **Russ, S.** **Lymphopenia following exposures of rats to 'soft' X-rays and the β-rays of radium.** *J. Exper. M.*, 1921, **34**, 271.

The authors found that 'soft' X-rays and β-rays of less penetrating power than the 'soft' X-rays produced an initial fall in the circulating lymphocytes, provided the blood be examined soon after radiation, and consider it important to remember that the lymphocytosis which occurs after a small or large dose follows a primary lymphopenia. A short account of the technique is given and two tables of results follow, which show a smaller percentage decrease after β-rays of radium than after 'soft' X-rays. The authors consider that this is probably due to the smaller penetrating power of the β-rays. P. L.-B.

Fraenkel, M. Röntgenstrahlenversuche an tierischen Ovarien zum Nachweis der Vererbung erworbener Eigenschaften und ihre Beziehungen zum Krebsproblem. [**Radiological researches on the ovaries of animals. Proof of the inheritance of acquired characteristics. Relations with the cancer problem.**] *Strahlentherapie*, 1921, **12**, 272. (*J. de radiol. et d'électrol.*, 1921, **5**, 429.)

The author has conducted a series of experiments on young or developing guinea-pigs, which may be described as follows: an animal was irradiated four times after birth. He states that it remained abnormally small, but gave birth in normal time to two young ones. These, not irradiated, remained still smaller, and gave birth to young ones which were sterile. The absence of hair on the head and back, provoked in the first generation by the irradiations, was repeated in the following generations. Autopsy of the animals showed a large accumulation of fat. Cystic degeneration of the ovaries was observed alike in the irradiated and non-irradiated animals.
S. U. L.-B.

Haas, Ludwig. Zur Frage der Abhängigkeit der Strahlenwirkung von Qualität und Quantität der Röntgenstrahlen. [**On the dependence of the action of X-rays upon their quality and quantity.**] *Strahlentherapie*, 1921, **12**, 838.

The author raises the question, which has been discussed by various other authors and attacked by several experimenters, whether the biological effects of X-rays depends upon the quality of the rays, i. e. wave-length as well as upon the quantity of radiation absorbed. Experiments by Friedrich and Krönig led them to the view that the effect upon the tissues depended solely upon the amount of X-ray energy absorbed and not at all upon the wave-length utilized. This result has not, however, found general acceptance, and it could hardly be anticipated by these authors themselves, that any generalization could be made from the limited number of tissues upon which they carried out their observations.

The author brings forward evidence that the X-ray effects do depend upon the wave-length selected as well as upon the quantity of radiation absorbed. A case of psoriasis was treated by X-rays, one region with unfiltered rays, a neighbouring part being given rays filtered by 1 mm. of aluminium, the dose in the latter case actually being a little less than in the former. Despite this, there was a more marked and favourable reaction of the condition to the filtered radiation, which, in the opinion of the author,

was to be attributed to the difference in the wave-length of the rays used. The article is illustrated by a photograph of the two regions, which show an appreciable difference in degree and character of reaction. S. R.

Hoffmann, Victor. Über Erregung und Lähmung tierischer Zellen durch Röntgenstrahlen. [**On the stimulation and destruction of animal cells by X-rays.**] *Strahlentherapie*, 1922, **13**, 285.

Hoffmann points out in this article that the evidence for stimulation by X-rays (smaller doses) is very much stronger in the case of vegetable tissues than in animal tissues. He cites the well-known experiments by various authors showing the increased growth of plants under suitable doses of radiation. These effects are generally much more striking than are shown by the low forms of animal life which have been subjected to similar experimental conditions.

The author has himself carried out experiments upon the eggs and larvae of *Rana fusca*, and these were exposed for various times to X-rays of different wave-length. Evidence of a stimulating action was obtained provided the dose of X-rays given was not too large. The author is careful to point out, however, that these stimulating effects may easily be missed if in the experimental conditions other variables have play. It is of interest to remark that the author observed a more intense action upon the organisms in question when soft X-rays were used than with filtered hard X-rays, equal quantities of radiation being used in the two cases. Over a more limited region of the X-ray spectrum Haas (vide *supra*) found that in a case of psoriasis exactly the reverse appeared to be true, a dose of short wave-length X-rays being more efficacious than a slightly larger dose of longer wave-length rays. S. R.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [B] after the title signifies that the original memoir contains a good bibliography of the subject dealt with.

REVIEWS

DISEASES OF THE LIVER

Epidemiology. Numerous writers, such as Brandenburg, Ehrmann, Gottstein, Hart, Henius, Kraus, Lepehne, Minkowski, and Schrader, have recently drawn attention to the great increase in frequency since the war of diseases of the liver, especially jaundice, acute yellow atrophy, and cholelithiasis (*vide* also *Medical Science*, 1921, **3**, 401–5). As the result of a questionnaire addressed to various medical clinics in Germany, Brandenburg, editor of the *Medizinische Klinik*, found that acute catarrhal jaundice and the severe forms of acute yellow atrophy were unusually frequent in certain towns of North Germany, whereas this was not the case in South Germany, or at least not to the same extent. Gottstein, an assistant at Umber's Clinic at Charlottenburg, states that a comparison of the statistics of his clinic for 1913 with those for 1920 brings out the following facts: (1) An increase in diseases of the liver from 3·2 to 4·7 per cent. of the total admissions. (2) A rise in the percentage of cases of jaundice among diseases of the liver from 19 to 38 per cent. (3) An absolute increase but unchanged percentage of cholelithiasis among the liver cases. (4) A decline in the number of cirrhosis cases from 26 to 20 per cent. of all the liver cases. Minkowski reports that simple icterus is three times as common as before, and that acute hepatitis without icterus is unusually frequent at the Breslau Medical Clinic. Various causes have been assigned for this increase such as war diet, deterioration of the food-supply, and the flooding of the market with preserved foods leading to gastro-intestinal catarrh and diminished power of resistance of the liver to injurious influences, the prevalence of infectious diseases, especially influenza, enteric fever, and spirochaetosis ictero-haemorrhagica, and the increase of syphilis, especially of cases treated with salvarsan. Gottstein, Kraus, and Minkowski, however, deprecate attaching too much aetiological importance to the increase of syphilis, on the ground that there is an unusual prevalence of diseases of the liver among persons in whom syphilis could be undoubtedly excluded. According to Gottstein only 30 of the 200 cases of diseases of the liver treated at the Charlottenburg Clinic in 1920 gave a positive Wassermann reaction, a history of syphilis and treatment by salvarsan. Ehrmann, who emphasizes the increased frequency of cholelithiasis, not only in adults but also in young persons, especially girls between the ages of 15 and 20, considers that the mechanical effect of a tight belt on an emaciated individual may be one of the factors responsible for the condition.

Symptomatology. According to Koch, of Reval, **hepatoptosis** of slight degree is relatively frequent. Examination of 1,038 persons, 394 of whom were males, and 644 females showed the presence of more or less marked hepatoptosis in 125 (10·4 per cent. of the males and 13 per cent. of the

females). Most of the cases were persons of middle age, a girl of 14 being the youngest and a man of 69 being the oldest. 100 out of the 125 cases presented no symptoms of their ptosis, 9 had diffuse local or radiating pain, and 1 had catarrhal jaundice. Cholecystitis was present in 15 cases or 12 per cent. of the cases of hepatoptosis, and in 27 cases, or only 3 per cent. of the 913 cases with a normal position of the liver. Koch attributes considerable importance in the diagnosis to the investigation of the posterior liver dullness. Disappearance of the lateral dullness is also a valuable sign.

Talentoni, of Leghorn, who records a case of wandering liver, remarks that in slight ptosis of the liver, which occurs with a certain frequency, the organ does not completely leave the diaphragm but usually sinks in association with it. The true wandering liver, on the other hand, is almost free in the abdominal cavity except posteriorly, where the ligaments are firmest. In the present case, which occurred in a nulliparous woman aged 74, the displacement of the liver which Talentoni attributes to congenital weakness of the hepatic ligaments, and of the falciform ligament in particular, was associated with a slight degree of jaundice due to torsion of the common bile-duct. Treatment consisted in the application of an abdominal bandage and the use of mild purgatives.

Tice and O'Conor, of the Washington Boulevard Hospital, report a case in a woman aged 55 of **Riedel's lobe of the liver simulating renal tumour,** the diagnosis being made by a ureteropyelogram, which showed the kidney to be in normal position with normal gross outline, and with a normal pelvis and calyx arrangement.

E. Weiss, of the Jefferson Medical College, Philadelphia, who reports a fatal case with the autopsy findings in a man aged 50, states that **aneurysm of the hepatic artery** is a very unusual condition, only 55 cases being on record. Infectious diseases, especially lobar pneumonia, play a larger part in its aetiology than syphilis. The main clinical features are pain, jaundice, and haemorrhage (haematemesis or melaena). A tumour, or bruit, is rarely present, and then only in the terminal stage. Under favourable circumstances the treatment is ligature of the hepatic artery.

According to Webster, **portal thrombosis** has been noted 21 times in the 6,050 autopsy records of the Johns Hopkins Hospital. It was found in 2·6 per cent. of the cases of cirrhosis of the liver, and was always accompanied by sclerotic changes in the walls of the portal vein or its branches. It was common in cases of carcinoma of the stomach or pancreas which had formed metastases in the liver and retroperitoneal glands. In 35 cases of cholangitis portal thrombosis was noted in 10·5 per cent.

Glaser reports a case of **dilatation of the portal vein** in a man aged 28, probably due to alcoholism, primary sclerosis of the vein being followed by saccular dilatation, which by compression of the common bile-duct led to congestion and dilatation of the bile-ducts and secondary biliary cirrhosis of the liver.

Hoover, of Cleveland, has collected 30 cases of **obstruction of the hepatic veins** that have been published since Budd's work in 1857. The ages of the patients ranged from 18 months to advanced life, and the duration of the symptoms from three days to thirteen years. The clinical symptoms are acute enlargement of the liver with a convex upper surface, increased resistance, rounded edge, and pain on pressure, and an ascitic transudate which is opalescent, contains numerous red cells, and does not readily clot on standing. The absence of any evidence of disease of the hepatic parenchyma

is also important. There is neither choluria nor cholaemia, and urobilin is not increased in the urine. If all sources of hepatic enlargement except venous stasis can be eliminated, the problem to be determined is whether the hepatic stasis originates from cardiac insufficiency, obstruction of the inferior vena cava above the ostia of the hepatic veins, or obstruction of the hepatic veins.

Under the name of **acute infective stomatogenous hepatosis** Pielsticker, of Essen, describes an acute enlargement of the liver characterized by subicterus, pain in the chest and abdomen, and almost universally associated with inflammation of the gums. The cases were first observed in the warm season at the end of June, increased in number in July, reached their height between the end of July and beginning of August, and then declined in frequency, no more cases being seen after the middle of September. 178 of the 211 cases seen occurred in miners. All forms of gingivitis were seen, from the catarrhal to the ulcerative type. Vincent's organisms, which Pielsticker regards as the cause of the condition, were found in the lesions of the gums.

According to Bihlmeyer, assistant at the Tubingen Children's Clinic, who records an illustrative case, the occurrence of **Distoma hepaticum** in the human subject has been very rarely described. Konjetzny stated that there were not quite 30 cases on record in 1910, since when no fresh cases, according to Bihlmeyer, have been published. The rarity of the occurrence is attributed by Bihlmeyer to the parasite being usually present only in small numbers, and therefore not causing any special symptoms. In many instances it is discovered only at the autopsy or by the presence of the ova in the faeces. The clinical symptoms are jaundice with enlargement of the liver due to obstruction to the flow of bile, cholecystitis, and cholangitis. Cases have also been described in which jaundice was absent. According to Inoye, most of the patients are more or less anaemic and frequently succumb with symptoms of purpura haemorrhagica. Bihlmeyer's patient was a girl aged 8 years, whose symptoms were progressive anaemia, loss of appetite, and apathy. The haemoglobin was 26 per cent., the red cells 2,370,000, the colour index 0·56, and the white cells 2,480. An eosinophilia of 17 per cent. roused the suspicion of helminthiasis and numerous ova of *Distoma hepaticum* were found in the stools. Anthelmintics had no effect, but recovery gradually took place, and thirteen months after admission the haemoglobin had risen to 69 per cent. and the number of the red cells to 4,080,000.

Guiart reports a case of *Fasciola hepatica* infection in man. The infection was possibly contracted in Salonika, and the symptoms were slight anaemia, enlargement of the liver, pain in the right side, and evening pyrexia. The eosinophilia was as high as 54 per cent., and was the immediate cause of a search for some parasitic disease. No drug was found to have any particular effect, except that calomel was followed by a positive finding when the stools had been several days negative.

Garnier and Reilly, who have observed more than 1,300 cases, adopt the following classification of cases of primary infective **jaundice**: (1) Spirochaetosis icterigenes, which includes all cases of infective jaundice, previously known as Mathieu's or Weil's disease. (2) Acute apyrexial jaundice, which is distinguished from the first group by certain clinical features. The onset is less distinct, and is not accompanied by myalgia. Although the icterus is usually very pronounced, the general condition remains satisfactory and the temperature keeps normal. The disease lasts from fifteen days to five weeks.

A special variety of this second group is relapsing jaundice. A short time after the first attack, in which the icterus is only slight and of short duration, the symptoms reappear in a severe form and last five or six weeks. Secondary infection of the bile-ducts may supervene and lead to the formation of abscesses in the liver or elsewhere. Acute apyrexial jaundice is also distinguished from spirochaetosis icterigenes epidemiologically, the former being equally frequent in all seasons, whereas the latter occurs chiefly in the summer and autumn. (3) Acute infective jaundice due to typhoid or paratyphoid bacilli. This is an uncommon form, its frequency being only 0·5 per cent. (vide *Medical Science*, 1921, **3**, 404). (4) Icterus gravis due to acute yellow atrophy of the liver, of which the writers have recorded four cases (*ibid.*, 1920, **1**, 598). (5) Mild infective jaundice of undetermined nature. (6) Epidemic and contagious jaundice, a seasonal disease occurring chiefly in the summer and autumn, of short duration and favourable termination.

Golay, of the Geneva Dermatological Clinic, records three cases of jaundice which developed from two to three months after injection of salvarsan in non-syphilitic patients. The Wassermann reaction was negative in all, the diseases for which they were being treated being lupus erythematosus, erythema multiforme, and soft chancre respectively. These cases show that syphilis has nothing to do with the appearance of jaundice after the use of arsenical preparations. Golay does not think that the jaundice was a mere coincidence and of the ordinary catarrhal variety, first, because he had not seen any case of jaundice which had not been preceded by injections of arsenical preparations; and, secondly, because the jaundice in each case appeared about the same time.

Pichler alludes to Eppinger's observation that a number of cases of jaundice have a peculiar odour of the breath resembling indol, which has led him to a correct diagnosis of icterus gravis. Pichler himself has noticed a similar odour about 20 times in 100 cases of catarrhal jaundice and about 90 cases of cirrhosis of the liver. As a rule, the odour was strongest when the jaundice was pronounced, being often absent at the onset, and first appearing when the jaundice became deep. In fatal cases the odour lasted until death. *Post mortem* it was no longer present, nor could it be detected in the urine, in spite of repeated examinations. It gradually disappeared in cases which recovered. Pichler never noticed the odour in dozens of cases of jaundice due to gall-stones or carcinoma of the liver and pancreas with obstruction of the bile-duct. He has, however, found it in a few cases of cancer of the stomach, even when there was no jaundice, and when no sign of liver disease could be detected during life or at the autopsy.

Behrend, of Philadelphia, reports a case of **acute yellow atrophy** in a girl aged 16 complicating acute appendicitis. Death took place on the third day after the operation. Behrend attributes the fatal complication to a late poisoning due to chloroform anaesthesia.

Lyon, of Cologne, records a case of subacute atrophy of the liver, in a woman aged 67, remarkable for the large quantity of free fluid (6 litres) in the abdominal cavity.

Miller states that for a number of years he has carefully investigated the history of every case of **cirrhosis** in his service at the Cook County Hospital, Chicago, and has never failed to obtain a history of marked alcoholism. Although prohibition, which was introduced in July 1919, has been far from complete in Chicago, as is shown by the number of cases of

acute alcoholism admitted, the amount of liquor consumed by the labouring classes has been greatly reduced. In 1920 there were only 19 cases of fatal cirrhosis admitted, all but one of which gave a history of chronic alcoholism as compared with 48 cases of cirrhosis admitted in 1919, 87 in 1918, and from 137 to 160 in each of the years 1910 to 1917. Miller concludes that portal cirrhosis, in the United States at least, is associated largely, and possibly entirely, with the use of alcohol.

Carillon devotes his Paris thesis to a consideration of remissions in the course of cirrhosis of the liver, applying the term only to those cases in which the remission has lasted at least two years. It points out that the appearance of a remission does not correspond to a complete anatomical recovery, which is indeed impossible. He begins as soon as the destructive lesions are checked, whether there be enough healthy liver tissue left or the parenchyma becomes regenerated by proliferation of the few cells which have escaped the sclerotic process. Clinically, the onset of a remission is shown by the disappearance of ascites.

Carillon recommends that diuretics and multiple punctures should be employed in order to diminish the obstruction of the portal vein. The thesis contains the histories of twelve cases, two of which are original, in which the duration of the remission ranged from two to twenty-four years.

As the result of his investigations Goldzieher has found that hypotrichosis, a large non-involuted pineal gland, a small basophilous and pigmented hypophysis, a small thyroid with atrophic parenchyma and increase of interstitial tissue, and marked diminution in size of the sexual glands are constantly present in hepatic cirrhosis. He concludes that individuals in whom a congenital constitutional deficiency is manifested by the presence of these anatomical features have such a feeble capacity for tissue regeneration, especially as regards the replacement of liver tissue, that hepatic cirrhosis readily develops in them as the result of various injurious influences. Lindemann also attaches much aetiological importance to the nature of the constitution in the development of cirrhosis.

For several years Fiessinger and Brodin have observed that cirrhosis of the liver, running an acute febrile course in alcoholic subjects, was always found at the autopsy to be associated with miliary tuberculosis of the peritoneum and lungs. The clinical history in such cases consists of two distinct stages, the first being one of alcoholic cirrhosis with ascites, and the second one of jaundice with insufficiency of the liver, aggravation of the nervous symptoms of alcoholism and a temperature ranging between 100·4 and 102·2. The first stage lasts from six to twenty months, and the second only a few weeks or even days. The writers record five illustrative cases, in two of which the miliary tuberculosis was almost exclusively peritoneal, in two was chiefly pulmonary, and in one renal. It was found that the tuberculin cuti-reaction was almost always negative in diseases in which there was a serious disturbance of the hepatic function. In incipient cirrhosis, in which there was no definite sign of hepatic insufficiency, the cuti-reaction was positive, but became negative when signs of insufficiency appeared. The cuti-reaction may therefore be regarded as of prognostic value as regards the progress of functional insufficiency in diseases of the liver. The writers attribute the absence of local reaction to tuberculin to the existence in hepatic subjects of an anergy similar to that met with in measles and typhoid fever. This anergy explains the development of

the terminal miliary tuberculosis in chronic hepatitis. It also explains how alcoholism favours the development of tuberculosis, as the liver undoubtedly plays a very important part in combating tuberculous infection.

Riesman, of Philadelphia, remarks that cirrhosis of the liver is one of the few chronic non-bacterial visceral diseases—perhaps the only one—that may actually be cured. In addition to two cases cured by Talma's operation he reports an example of a spontaneous cure in an alcoholic man aged 57, which was due to a fibrinous peritonitis following the last tapping. The adhesions resulting from this peritonitis constituted a spontaneous Talma operation, and sufficed to establish an adequate collateral circulation.

According to Lindemann, of Berlin, who records a case in a male infant aged 5 months, secondary biliary cirrhosis is extremely rare in infancy, and hitherto cases of the kind, apart from syphilis, tuberculosis, and aplasia or malformation of the bile-ducts, have been reported only by Bossert, Cornelia de Lange, and Pearce. Lindemann excludes syphilis and other infectious diseases, such as melaena, as factors in his own case, and attributes the condition to a constitutional inferiority of the liver, which was thereby rendered susceptible to an ascending inflammation from the intestine caused by a defective state of the intestinal epithelium which was either congenital or due to the products of metabolism.

Lereboullet and Mouzon report a case of bronzed diabetes in a man aged 42, who did not develop diabetes until 45 months after the melanodermia and 28 months after the first examination, in the course of which considerable enlargement of the liver was detected. Four years after the onset of the disease glycosuria, persistent thirst, polyuria, and polyphagia developed. The diabetes then ran a rapid course, ending in $3\frac{1}{2}$ months in acidosis and coma accompanied by ascites and enormous oedema of the lower limbs. The remarkable feature in this case was the late appearance of diabetes. In the great majority of cases of bronzed diabetes, pigmentation, enlargement of the liver, and glycosuria have appeared simultaneously. In other instances glycosuria has been the first symptom noted, and the pigmentation has been secondary. The writers do not know of any other case in which it could be so definitely affirmed that the glycosuria had appeared secondary to hypertrophic pigmentary cirrhosis. Commenting on this case, Achard and Leblanc maintain that in the syndrome of bronzed cirrhosis there is a constant element, viz. a lesion of the liver, which is usually cirrhosis without any special features apart from iron pigment, and a variable element consisting of two dystrophic syndromes, viz. a disturbance of the evolution of the pigment and a disturbance of glycolysis. Any of the three elements, diabetes, cirrhosis, or pigmentation, may appear first, or diabetes and melanodermia may be absent. Achard and Leblanc record a fatal case with the autopsy findings in a man aged 55 in which bronzed cirrhosis was not accompanied by any glycosuria.

Carcinoma. Catsaras, of the Athens Medical Faculty, remarks that metastases in the skeleton are extremely frequent in cancers of the breast and prostate, fairly frequent in cancer of the thyroid and hypernephroma, and less frequent in cancer of the uterus, gall-bladder, intestine, and oesophagus. Primary adenocarcinoma of the liver rarely gives rise to metastases, and when it does it selects the lymphatic glands at the hilum of the liver or the lungs. These metastases may sometimes have a greenish coloration due to the production of bile by the cells of the growth. Catsaras records a fatal case in a man aged 65, in whom hepatic cirrhosis was

associated with primary adenocarcinoma of the liver and a metastasis in the upper end of the femur, where it gave rise to a subtrochanteric fracture. With the exception of a case reported by Schmidt, Catsaras has been unable to find a similar case on record.

Boscemi, of Florence. records two cases of primary carcinoma of the liver in pregnancy. The first case occurred in a woman, aged 37, in whom the hepatic tumour was associated with mitral stenosis and incompetence, ankylostomiasis, and a pleural effusion probably due to the growth. Abortion was induced in the sixth month of pregnancy. The subsequent history is not recorded. The second case was that of a woman, aged 38, in whom spontaneous abortion occurred in the fifth month of pregnancy, followed by death the next day. Primary carcinoma of the liver with secondary growths in the lungs was found *post mortem*. The cases show that carcinoma of the liver, like many other cancers. although situated at a distance from the genital organs, is aggravated by the mere fact of pregnancy, while the effect of cancer of the liver on pregnancy was shown by the spontaneous abortion in one case.

Appel states that until a few years ago it was generally held that malignant growths were very rare in negroes. Although this opinion is incorrect, it is true that all forms of malignant tumours are not equally common among them. While cancer of the stomach is rare, multiple adenocarcinoma of the liver is comparatively common in negroes. During the period 1916–19 Appel observed four cases of this tumour, two in men and two in women aged from 20 to 40, at the native hospital at Santa Isabella in Fernando Po. It was not certain whether the growth had originated in the liver-cells or in the bile-ducts, but the latter were the most probable origin.

Judd, of Rochester, Minn., agrees with Graham that **cholecystitis** rarely exists without hepatitis. Often the hepatitis is so slight that it is overlooked unless a special examination is made. Out of a total number of 1,290 gall-bladder and bile-duct cases, Judd found that 347 or 26·8 per cent. had associated pancreatitis, the infection being probably caused by way of the lymphatics from the gall-bladder. He suggests that the incomplete relief of symptoms and the recurrences in a small number of these cases are due to inflammations in the liver and pancreas.

Lehmann, of the Rudolf Virchow Hospital at Berlin, records his observations on 40 cases of **cholelithiasis** in women whose ages ranged from 27 to 69. In three cases the mother and in one case the brother had suffered from undoubted cholelithiasis, while in one case the mother had had gastric or duodenal ulcer. In 32·5 per cent. mental worry, in 2·5 per cent. tight lacing, in 2·5 per cent. parturition, and in 7·5 per cent. trauma were given as the cause of the attack, while in 55 per cent. no cause could be found. 40 per cent. had suffered from constipation. In 4 or 10 per cent. there was a history of typhoid fever from 1 to 37 years previously. 30 or 75 per cent. had been healthy, especially as regards their gastric condition until their first attack; 5 or 12·5 per cent. had had an undoubted peptic ulcer, 4 or 10 per cent. had suffered from appendicitis, and 1 or 2·5 per cent. from colitis. A more or less definite enlargement of the liver was found in 80 per cent. Examination of the secretory function of the stomach showed hyperchlorhydria in 37·5 per cent., normal secretion in 35 per cent., and complete achlorhydria in 27·5 per cent. The largest proportion of cases of hyperchlorhydria and normal secretion was found in recent attacks,

while the long-standing cases with chronic cholecystitis showed achlorhydria. Examination of the motor activity of the stomach showed a normal condition in 87·5 per cent., and distinct retention in 12·5 per cent.

Friedman, of New York, emphasizes two points often ignored in practice, viz.: (1) that gall-stones are often apparently symptomless, and (2) that the correct diagnosis of this condition is possible. He divides cases of cholelithiasis into three groups: (1) those with typical attacks of pain; (2) those in which the paroxysms of pain are atypical; and (3) those in which the element of pain is entirely absent, but dyspeptic and nervous symptoms predominate. He points out that pressure-tender points in the intercostal spaces at the level of the gall-bladder in the continuation of the right axillary, scapular, and posterior median line are almost always found in persons suffering from diseases of the gall-bladder, even when tenderness in the gall-bladder region proper cannot be elicited. The presence of these tender spots, which Friedman regards almost as characteristic as the history in the group of so-called typical cholelithiasis, is attributed by him to the fact that gall-stones are rarely aseptic, and that there is as a rule a concomitant cholecystitis.

Ramond, Jacquelin, and Borrien describe the following three minor signs of cholelithiasis which they have investigated at the Hôpital Saint Antoine, Paris, during the last two years: (1) The xiphoid point. Tenderness over the xiphoid cartilage is hardly ever absent. As an isolated sign it may be present in painful processes connected with the cardiac end of the stomach, in emphysema, dilatation of the heart, and pericarditis, but in association with a tender spot over the gall-bladder it is presumptive evidence in favour of a more or less latent cholelithiasis. (2) The respiratory sign. This consists in a definite diminution of the vesicular murmur at the right base, especially in the posterior axillary line in the course of cholelithiasis; sometimes this sign is found in the middle lobe and even in the upper part of the right lung. It may persist for months after an attack of biliary colic. (3) Reflex pain at the site of emergence of the anterior branches of the right intercostal nerves. The pain is rarely spontaneous, but is readily produced by light percussion. As this sign is sometimes met with in gastric ulcer of the lesser curvature, it possesses less diagnostic value than the respiratory sign.

The liver in pregnancy. Labbé, Hutinel, and Nepveux (1) (2), who record two illustrative cases in women aged 24 and 26, consider that hepatic insufficiency plays the chief part in the toxaemia of pregnancy and especially in forms accompanied by acidosis. They maintain that a study of the hepatic function is quite as important as an examination for albuminuria, and that when a systematic examination of the urine is made in pregnancy, cases of hepatic insufficiency will be found to be more frequent than has hitherto been supposed. The affection of the liver in the writers' cases was shown by the presence of well-marked acidosis, urobilinuria and proteolytic insufficiency.

Crainicianu and Popper, of Bucharest, examined 47 pregnant women, the majority of whom were in the last month of pregnancy, and found that 20 per cent. of them at this stage, in spite of the absence of any disease which could have affected the liver, presented urological signs of biliary retention, and that 33 per cent. had digestive haemoclasia, which indicated hepatic insufficiency. In addition to those cases in which hepatic insufficiency could be detected only by delicate tests, some of the women presented

various forms of jaundice, including icterus gravis. The writers recommend that the pregnant woman should seek to avoid all sources of intoxication, and suggest that the urinary signs of hepatic insufficiency, as well as haemoclasia, should be sought for from time to time during pregnancy. Chloroform should not be employed, owing to its deleterious effect upon the liver, but ether and oxygen should be preferred as anaesthetics.

Tests of hepatic function. As will be seen from the papers of Bauer, of Vienna, Crainicianu and Popper, of Bucharest, Holzer and Schilling, of Chemnitz, Kisch, of Marienbad, Mauriac, of Bordeaux, Oddo and Borie, of Marseilles, Powilewicz, of Paris, and Retzlaff, Sömjén, and Schiff and Stransky, of Berlin, much has been written lately on Widal's test of hepatic function, which is known by the name of the 'haemoclasic crisis'. The test consists in the administration of 200–300 gm. of milk, a positive reaction or haemoclasic crisis being shown by a leucopenia with predominance of the lymphocytes, a fall of blood-pressure and great changes in coagulability and in the refractrometric index of the serum. Holzer and Schilling, who employed the test in 60 cases, all of which were in adults, obtained a positive reaction in all obvious diseases of the liver, such as carcinoma, jaundice, and cholelithiasis. In typhoid, paratyphoid B, scarlet fever, measles, and tuberculosis they also obtained a positive reaction, except in one case of severe tuberculosis, and one of paratyphoid B, which showed a definite leucocytosis. They also found a positive reaction in cases of heart disease, cases undergoing salvarsan treatment, and in cases of subacidity and anacidity. Several observers such as Bauer, Holzer and Schilling, Kisch and Mauriac, found that the leucopenia was the only constant element of the haemoclasic crisis, and was not always accompanied by a fall of blood-pressure or the other phenomena mentioned. According to Mauriac the test is inapplicable in children, in whom the ingestion of very small quantities of milk is sufficient to cause a digestive leucopenia in health. The same view is held by Schiff and Stransky, who used the test in 90 infants, some of whom were normal and others were suffering from various affections, including diseases of the liver. With the exception of four cases in which a transient leucocytosis occurred, all reacted with a leucopenia twenty minutes after taking the milk. Sömjén, who employed the test in 82 cases, draws special attention to the rapid appearance and still more rapid disappearance of the reaction. In about half the cases with a positive reaction he found that within 40 minutes the leucopenia was replaced by leucocytosis. The leucopenia ranged from 20 to 60 per cent., but did not bear a direct relation to the severity of the hepatic disturbance, as on two occasions an enormous leucopenia was observed after slight massage of the liver. Sömjén considers that the ingestion of milk and massage of the liver both act in the same way, viz. by causing a reflex stimulation of the liver, and probably of the duodenum and upper part of the jejunum.

Powilewicz, in his Paris thesis, in which he records 30 illustrative cases, states that the test of digestive haemoclasia is always positive in the toxaemia of pregnancy which is manifested by albuminuria, hypertension, eclamptic convulsions, and retinitis. He found that in pregnant women without any signs of toxaemia the test was positive, on the average, in one out of two cases, though less marked than in toxaemia. These apparently normal women, therefore, had a latent hepatic insufficiency which was revealed by the test of digestive haemoclasia. In such cases a general

anaesthetic should be avoided as far as possible, as well as all analgesics and hypnotics.

Oddo and Borie record 9 cases consisting of one of biliary cirrhosis, and eight of various forms of jaundice in which, as the result of hepatic opotherapy, i. e. administration of powdered liver in doses of 2 gm. a day, there was a complete though transient disappearance of the haemoclasic crisis. They point out that the practical importance of their investigations lies in the fact that a certain number of cases of hepatic insufficiency following chloroform anaesthesia and the arsenical treatment of syphilis could be prevented by prophylactic administration of powdered liver before the operation or injection of arsenobenzol, and for a few days afterwards.

According to Spence and Brett, a valuable indication of the efficiency of the liver can be obtained by estimating the changes in blood-sugar concentration which follow the ingestion of laevulose. In a healthy adult with a normal liver efficiency a dose of 50 gm. laevulose will produce no appreciable rise in blood-sugar, while in a subject with diminished liver efficiency a definite rise in blood-sugar will result from the ingestion of laevulose. The height and length of the blood-sugar curve which portrays this rise will be in proportion to the degree of liver inefficiency. The test affords a means of estimating the degree of liver damage in cases of toxic salvarsan, hepatitis, and other diseases of the liver. The kidney threshold for laevulose is lower than that for glucose, and varies in different individuals. This inconstancy of the threshold for laevulose renders the older method of testing liver inefficiency by urinary examination inaccurate.

Treatment. Lyon's method of non-surgical biliary drainage has attracted considerable attention in the United States, as is shown by the papers of Bassler, Luckett, and Lutz, Crohn, Reiss, and Radin, Einhorn (1) (2), Friedenwald and Morrison, Smithies, Karshner, and Oleson, and S. Weiss. The method is based on Meltzer's discovery of the fact that a solution of magnesium sulphate, when introduced locally into the duodenum, will relax the tonus of the duodenal wall and the sphincter of the common bile-duct, and that almost simultaneously with this relaxation the gall-bladder will expel its fluid contents, partially or wholly into the duodenum. Immediately after the publication of Meltzer's paper, Lyon showed that the localization of magnesium sulphate in various strengths in the human duodenum would promptly deliver bile through the duodenal tube in various strengths and quantity. The bile obtained by the tube undergoes certain definite changes in colour and viscosity, being first a light lemon to golden yellow, then a deeper, richer, more syrupy golden yellow, and finally a uniformly light lemon yellow. The scope of the method as set forth by Lyon in a paper written in collaboration with Bartle and Ellison, based on a series of over 400 cases, is first as a means of diagnosis of biliary diseases to supplement the usual clinical and roentgenological methods, secondly as an alternative method of treatment of many types of gall-bladder and duct diseases, and thirdly as a supplementary post-operative method in cases incompletely cured by operation alone. Smithies, Karshner, and Oleson, of Chicago, maintain that the method is contra-indicated in obstructive lesions such as calculi, tumours, &c., when more logical and positive relief may be obtained by operation. They regard the method as of value in the following groups of cases: (1) acute choledochitis, cholecystitis, and hepatitis in association with acute infections (scarlet fever, pneumonia, typhoid, tonsillitis), or arising as limited biliary tract disease. (2) Hepatitis with duct malfunction of toxic

origin, ptomaine poisoning, plumbism, or phosphorus poisoning, and acute yellow atrophy, especially the variety occurring after therapeutic injection of arsenical products. (3) Biliary stasis with acute or chronic heart embarrassment. (4) Bile-tract stasis in cirrhosis or severe anaemia. (5) Dyspeptic stasis occurring as biliousness associated with migraine, epilepsy, &c. (6) Chronic or acute 'rheumatoid' infections. (7) Bile-tract or liver stasis or infection present in diabetes, exophthalmic goitre, or pancreatitis when operation is impossible. (8) Duodeno-pyloric or pyloric ulcer. (9) Intestinal stasis complicated by dyspepsia of bile-tract and liver type. (10) Bile-tract stasis with low grade indolent infection not complicated by gross mechanical defects, calculi, or tumours.

Friedenwald and Morrison, of the University of Maryland, employed Lyon's method in 315 cases and came to the conclusion that it gave valuable aid in the diagnosis of gall-bladder affections, especially before the appearance of complications. Not only do they regard it as an important means of determining the presence of focal infection in the gall-bladder, but they also found it extremely valuable in the treatment of catarrhal jaundice, biliary stasis, and gall-bladder infections, as well as helpful in relieving the infection which may remain after operations on the gall-bladder. On the other hand, Bassler, Luckett, and Lutz, and Crohn, Reiss, and Radin, of New York, are less enthusiastic. The former group of writers regard the method as a poor substitute for operation. Though it may be employed in suitable cases, as a temporary measure, they maintain that it should not be depended upon to correct or definitely to benefit diseased gall-bladders or when gall-stones exist.

Crohn, Reiss, and Radin, while admitting that the subject is entitled to much consideration, state that they did not succeed in utilizing the diagnostic test for the identification of cases of chronic gall-bladder disease.

According to Einhorn (1) (2), who has made numerous studies on the action of various salts and other substances on the liver after their introduction into the duodenum, many more valuable hints regarding gall-bladder lesions may be obtained from examination of the natural fasting bile than from the bile obtained after stimulation by magnesium sulphate. In cases of jaundice, however, in which no bile is found in the fasting state, Einhorn recommends that a liver stimulant should be injected into the duodenum to ascertain whether the increased flow of blood from the liver is still able to push through some of its products into the duodenum.

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J. D. R.
G. W.

INTESTINAL PARASITES [1]

Pringault states that apart from certain mining regions where ascariasis or ankylostomiasis is prevalent, intestinal parasites have attracted little attention in France. During the last three years he has examined 948 stools from patients in various hospitals at Marseilles with the following results: Intestinal parasites were relatively frequent in children and much less common in the stools of elderly persons. As a general rule they were rarely found in stools of normal consistence. Protozoa, which were commonest in adults, were found in the following order of frequency: (1) *Amoeba coli* in 9·01 per cent. (2) *Amoeba dysenteriae* in 4·66 per cent. (3) *Lamblia intestinalis* in 2·96 per cent. These parasites were most frequent in adults, and in the summer were found in one-third of the cases of diarrhoea. (4) *Trichomonas intestinalis* was chiefly found in the stools of children suffering from diarrhoea. (5) In five instances the spirilla described by Le Dantec were found in large quantities. Worms were found in the following.

[1] The names employed for the various parasites are those used by the original authors. In many cases they are not in accordance with correct modern nomenclature, e. g. *Entamoeba histolytica* is referred to both as *Amoeba dysenteriae* and *Entamoeba dysenteriae*.

order of frequency: (1) *Oxyuris vermicularis* in 11·87 per cent. (2) *Trichocephalus trichiurus* in 8·16 per cent. (3) *Ascaris lumbricoides* in 8·15 per cent. (4) *Taenia saginata* in 2·54 per cent. (5) *Bothriocephalus latus* in 0·21 per cent. (6) *Taenia solium* in 0·10 per cent.

Peiser examined 638 bodies of all ages and both sexes at the Pathological Institute of the Augusta-Victoria Hospital, Berlin, and excluding children under two years in whom no parasites whatever were present, found worms in 139 cases or 26·53 per cent. out of 524 bodies. 85 cases or 16·22 per cent. had oxyurides, 32 or 6·11 per cent. trichocephali, 13 or 2·48 per cent. ascarides, 8 or 1·53 per cent. taeniae, and 1 or 0·19 per cent. *Pentastomum hepaticum*. The highest percentage of parasites—41·38 per cent.—was found in children between 2 and 14 years of age, the incidence in men being 31·03 per cent. and in women 21·92 per cent. In children oxyurides were found in 34·48 per cent. and ascarides in 6·90 per cent. The comparative rarity of ascarides and taeniae was due to the fact that these parasites are particularly susceptible to treatment and had mostly been removed during life by anthelmintics. In none of the cases was there any connexion between the cause of death and the presence of the worms.

Popowski investigated the faeces of 890 persons, consisting of 292 men, 417 women, and 181 children, suspected to have tapeworm. Intestinal parasites were found in 515 cases or 57 per cent., viz. *Trichocephalus dispar* in 455 cases or 51 per cent., *Ascaris lumbricoides* in 20 cases or 2·2 per cent., *Bothriocephalus latus* in 6 cases or 0·7 per cent., *Taenia solium* in 6 cases or 0·7 per cent., *Oxyuris vermicularis* in three cases or 0·3 per cent., *Ascaris lumbricoides* and *Trichocephalus dispar* in 18 cases or 2·0 per cent., *Taenia solium* and *Trichocephalus dispar* in 4 cases or 0·4 per cent., *Bothriocephalus latus* and *Trichocephalus dispar* in 2 cases or 0·2 per tent., and *Ascaris lumbricoides, Trichocephalus dispar*, and *Taenia solium* in 1 case or 0·1 per cent. The presence of blood as detected by the phloridzin and benzidine test was found in 106 cases of *Trichocephalus dispar* or 23 per cent., in 15 cases of *Ascaris lumbricoides* or 75 per cent., in 2 cases of *Bothriocephalus latus* or 33 per cent., in 1 case of *Taenia solium* or 17 per cent., in 7 cases of *Ascaris lumbricoides* and *Trichocephalus dispar* or 40 per cent., and in 1 case of *Bothriocephalus latus* and *Trichocephalus dispar* or 50 per cent. In all the other cases the blood test was negative. Among 375 cases in which no intestinal parasites were found the blood test was positive in 54 or 14 per cent. The presence of blood in the stools is therefore not characteristic of *Trichocephalus dispar*, as it occurs only 9 per cent. more frequently in such cases than in those in which no intestinal parasites are found.

Jung and Sell examined 380 stools at the Munich Bacteriological Investigation Department with the following results: 139 or 36·75 per cent. contained the ova of worms or protozoal cysts or both, and 241 were negative. The highest percentage of carriers was found in those living in country districts. The ova of worms (*Ascaris lumbricoides, Trichocephalus dispar*, and *Oxyuris vermicularis*) were found in 20·78 per cent., and protozoal cysts (*Entamoeba coli* and *Lamblia intestinalis*) in exactly the same percentage.

According to Leger, the natives of French Guiana are infested with intestinal parasites in a high degree. In 1917 he examined the stools of 274 recruits aged from 18 to 34, and found that 82·7 per cent. were carriers of one or more worms, viz. *Ankylostoma* in 62 per cent., *Trichocephalus dispar* in 41 per cent., and *Ascaris lumbricoides* in 38 per cent., or a total infestation

of 140 per cent. (349 parasites to 242 subjects). He has recently made investigations in Cayenne on 92 healthy children aged from 1 to 12 years, and found that 70 per cent. were infested. In 39 cases the faeces contained the ova of a single worm or protozoon, viz. *Ascaris lumbricoides* in 26, *Trichocephalus dispar* in 7, *Entamoeba dysenteriae* in 3, *Necator americanus* in 2, *flagellata* in 1. In 18 cases 2 parasites and in 8 cases 3 parasites were present. Although the incidence of intestinal parasites is higher in Cayenne than in the Algerian localities examined by Soulié and Derrieu, typhoid and paratyphoid infections have always been very rare and the water supply is remarkably pure. Leger therefore does not accept the contention of Soulié and Derrieu that the degree of water pollution can be estimated by the parasitological index without a bacteriological examination being necessary.

Müssig, of Darmstadt, remarks that the alarming increase in ascariasis among all ages and classes of society in Germany since the war is connected with the prevailing lack of cleanliness and an almost exclusively vegetable diet (vide also *Medical Science*, 1921, **4**, 105). He records three cases of severe ascariasis, the first of which simulated ruptured tubal gestation and was fatal, the second resembled the nervous and gastro-intestinal form of influenza, and the third was associated with gall-stones. He points out that in addition to mechanical factors, which undoubtedly play an important part in the damage to the carrier, and the loss of food and blood caused by the parasite, toxic factors must be taken into consideration. In ascariasis there is not only one poison at work, but there are numerous pharmacologically active substances which may produce different symptoms in individual cases.

Gaudier, of Paris, records a case in a woman aged 28, showing that the presence of ascarides in the intestine may cause disturbance simulating severe surgical symptoms requiring operation, whereas such cases are readily cured by simple medical treatment. During the recent war the civilian population was infected by the colonial troops, and severe cases of ascariasis occurred, like those usually seen only in the tropics, and characterized by complications such as intestinal obstruction, perforative peritonitis, reflex nervous disturbances, and symptoms due to migration of the worms to other organs such as the gall-bladder, appendix, &c. The only definite proof of helminthiasis is the presence of ova in the stools or the expulsion of a worm. The other signs, which have only the value of presumptive evidence, are eosinophilia, which may range from 5 to 72 per cent., the presence of blood in the stools, periumbilical colic of a nocturnal type, atypical dyspepsia, recurrent nausea and diarrhoea, and reflex or vasomotor disturbances such as pruritus, urticaria, inequality of the pupils, paroxysmal cough, and asthmatiform attacks.

Glock also reports a case of severe ascariasis in a woman aged 45, whose symptoms resembled gall-stone colic, probably owing to one of the worms getting into the common bile-duct, and Botelli, of Milan, records two fatal cases in children aged 4 and 2 years respectively of multiple abscesses of the liver due to ascarides. In neither case was there ascites or jaundice.

Villar, Philip, and Soubiran, of Bordeaux, report a case of recurrent intussusception of the ileum in a boy aged 9 years infested with ascarides. Death occurred two hours after the operation. The writers attribute the intussusception to excessive peristalsis of a segment of the bowel due to the ascarides, and the death to toxaemia secondary to hepatitis. They maintain

that this case, though rare, is not unique, and declare that many children in France lose their lives every year owing to the failure to recognize such a complication of intestinal parasitism.

Helminthiasis, as a cause of dysmenorrhoea, especially infestation by *Ascaris lumbricoides* or *Oxyuris vermicularis*, is described by Leo, who attributes considerable diagnostic value to Coullaud's sign, i.e. enlargement of the fungiform papillae (vide *Medical Science*, 1921, **4**, 103), and recommends the administration of anthelmintics when dysmenorrhoea is accompanied by this sign.

Breinl examined the blood of 150 hookworm infested white children in North Queensland, aged from 7 to 15 years, and found that the average Arneth index in the hookworm infested child showed a decided shift to the left. Though the significance of the shift of the Arneth index to the left is still uncertain, Breinl suggests that in such diseases as hookworm infection and malaria, in which the destruction of red cells goes for a time at least hand in hand with an increased activity of the blood-forming organs, the increased activity extends to the new formation of leucocytes, and consequently a greater number of young leucocytes are met with in the peripheral blood. A differential count indicates that in young children between the ages of two and four years the relative number of polymorphonuclear neutrophil leucocytes is decreased, whereas that of the lymphocytes is increased. After the seventh year the relative proportion of the various forms of white blood corpuscles is fairly constant. As was to be expected, the relative increase in the number of eosinophils was well pronounced throughout the series of counts.

Lemierre and Lantuéjoul record a case of ankylostomiasis in a man aged 58 remarkable for the evolution of the eosinophilia. Before treatment it was 16 per cent.; 6 days after the first administration of thymol it rose to 25 per cent., and after the second dose of thymol it oscillated between 23 and 25 per cent., to reach its culminating point—37 per cent.—at the end of about three weeks. For another three weeks it remained between 23 and 27 per cent., and then gradually fell; five months after treatment it was still between 7 and 8 per cent. The increase in the eosinophils after treatment, which was so marked though temporarily a feature in this case, is not exceptional, as is shown by cases reported by Boycott.

Kofoid and Tucker investigated the relationship of infection by hookworm to the incidence of morbidity and mortality in 22,842 men of the United States Army at Camp Bowie, Texas, from October 1917 to April 1918, with the following results. It was found that sickness, whether mild or severe, acute or chronic, was increased among the men who were weakened in general health by hookworm infection. Infected men showed in particular an increased susceptibility for tonsillitis, laryngitis, pneumonia, and measles. The mortality in 10 heavily infected organizations in which hookworm infection was above 10 per cent. was 1·5 per cent., whereas in 7 more lightly infected organizations the death-rate was 0·8 per cent. Hookworm infection was relatively higher generally in hospital patients, among delinquents, and in venereal isolation camps than in camps as a whole. The writers conclude that from the standpoint of economy and efficiency it would be more profitable to eliminate hookworm infection from every soldier, as he enters the service, than to allow him to continue untreated.

Rojas and Morengo, of Guayaquil, Ecuador, record nine cases in which hookworm infection caused nephritis with chloride retention. The index of

urea excretion was low in three cases. Return to normal took place as soon as the hookworms were removed by anthelmintic treatment, although the red count was still low.

As the result of their experiments with the administration of chenopodium in hookworm disease, Darling and Smillie, of the Laboratory of Hygiene of the São Paulo Faculty of Medicine, have come to the following conclusions: (1) A preliminary purge does not add to the efficiency of the treatment with chenopodium, 1·5 c.cm. being considered the adult dose; (2) so far from a preliminary starvation period being necessary in the treatment of hookworm disease with chenopodium in divided doses of 1·5 c.cm., its efficacy is lessened thereby; (3) a small amount of food given at the same time as the drug when the chenopodium is administered in divided doses of 1·5 c.cm. greatly diminishes the efficacy of the drug in the treatment of hookworm disease; (4) in the smaller doses of chenopodium that are given to children, the decrease in efficiency of the drug caused by preliminary purgation, starvation, or food is much more striking than with the full adult dosage of 1·5 c.cm.

Caius and Mhaskar, whose previous articles have been recently noticed (vide *Medical Science*, 1920, **4**, 106) have continued their series of papers in connexion with the hookworm inquiry in the Madras Presidency on the correlation between the chemical composition of anthelmintics and their therapeutic value. As the result of their observations on oil of turpentine, male fern, kousso, kamala, and pulvis arecae, they come to the conclusion that none of these drugs could be recommended as anthelmintics.

According to Hall, senior zoologist to the United States Bureau of Animal Industry, who made a series of investigations on himself as well as on dogs, horses, and swine, carbon tetrachloride is apparently more effective, safer, and cheaper than the drugs used at present to remove hookworm. It appeared to be of no value for removing tapeworms, and was as unreliable as other anthelmintics for removing whipworms. The effective dose was 3 c.cm. given in hard capsules.

Calvin, of Chicago, remarks that native infestation with the broad tapeworm *Diphyllobothrium latum*, although fairly frequently reported in the United States, has mostly occurred in immigrants who have acquired the infection abroad. In addition, however, to five cases previously reported, in which the patient undoubtedly acquired the parasite in the United States (Minnesota or North Dakota), he records two cases in children aged 7 and 3 years respectively, who had never been out of Chicago. The most efficient drug for the expulsion of the worm is male fern.

According to Cordes, of the Hamburg Institute of Marine and Tropical Diseases, who successfully treated a case of *Balantidium* colitis by intravenous injection of emetine hydrochloride, emetine has the same action on balantidium colitis as in amoebic dysentery, although the causal protozoa do not belong to the same class. The patient observed by Cordes received in all 0·6 gm. emetine, the discharge of balantidia ceased in 8 days, in 15 days the intestinal ulcers were found to be healed on rectoscopic examination, and the patient could be regarded as cured two months after the commencement of treatment.

According to Deschiens, who devotes his Paris thesis to a consideration of *Lamblia* or *Giardia* enteritis, the essential features of this condition are its extreme tenacity and the occurrence of successive attacks. Clinically three types may be described, viz.: (1) the dysenteric type, which usually

constitutes the first stage of infestation, but may also occur as an acute episode in chronic lambliasis. This type was observed during the war in Flanders, Gallipoli, Egypt, Salonica, and certain sections of the French front. (2) The chronic type, which is characterized by its extreme obstinacy, remittent or intermittent diarrhoea, and occurrence of successive attacks. (3) The incomplete type (*formes frustes*) which forms a transition between those who are merely carriers and those severely infested. In such cases the attacks of diarrhoea are rare and of slight intensity, the number of parasites in the stools is scanty, and there are long negative phases. During the war lambliasis was frequently associated with amoebiasis. The latter was often cured by specific treatment, but the colitis persisted owing to lambliasis proving refractory to treatment. Association of *Lamblia* with other intestinal flagellata such as *Tetramitus, Trichomonas,* or *Cercomonas* does not produce a different clinical picture from that of pure lambliasis. The prognosis of lambliasis should be guarded owing to its obstinate character, which, as De Buen points out, is due to the deep penetration of the parasite into the intestinal wall, the possibility of hyperacute symptoms developing at any stage, and such sequelae as paracoecal abscess. Death may be caused by *Lamblia* dysentery or cachexia. McGill, of Butte, Montana, who agrees with Deschiens and De Buen that no treatment has yet been discovered for ridding the bowel of *Giardia,* states that the parasite may invade the gall-bladder and duodenum, where it may give rise to symptoms resembling duodenal ulcer.

Maxcy, of the Department of Medical Zoology of the School of Hygiene and Public Health of the Johns Hopkins University, examined 89 children admitted to Howland's Clinic at the Johns Hopkins Hospital. With few exceptions they were suffering from acute infectious diseases, and free from gastro-intestinal disturbance. 18 cases or 20 per cent. were found to be harbouring protozoa of some type, the relative frequency of the parasites being as follows: *Giardia intestinalis* 10 cases; *Giardia* and *Entamoeba coli* 1; *Giardia* and *Blastocystis* 2; *Giardia, Hymenolepis mana,* and *Oxyuris vermicularis* 1; *Entamoeba coli* 4. Maxcy's conclusions are as follows: (1) *Giardia intestinalis* is present in the intestinal tract of a large percentage of apparently normal children; (2) it is rarely found before the first year; (3) the percentage of infestations appears to be much higher in childhood than in adult life; (4) the finding of a large number of motile *Giardia* in a diarrhoeic or dysenteric stool is not sufficient evidence to establish the aetiological relationship of this parasite. In certain rare instances the parasite may be responsible for some intestinal disturbance, though this point has not yet been firmly established.

A case of lambliasis complicated by chronic arthritis and successfully treated by duodenal biliary drainage is reported by Lyon, Bartle, Ellison, and Richardson, of Philadelphia.

Carr and Chandler, of Lansing, Michigan, and Reverdin and Chomé, of Geneva, report cases of lambliasis successfully treated by intravenous injection of novarsenobenzol.

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J. D. R.

SOME RECENT WORK ON THE SYMPTOMATOLOGY AND PATHOLOGY OF THE CORPUS STRIATUM

In previous numbers of *Medical Science* (1920, **1**, 143, and 1921, **3**, 353) the two earlier papers of C. and O. Vogt on the pathological anatomy of diseases of the corpus striatum have been briefly abstracted. These authors have now published a large monograph embodying the detailed description of their pathological and clinical material and their conclusions on the symptomatology of corpus striatum lesions. Thirty-three cases are described in great detail and their pathological anatomy illustrated by a large series of the most exquisite micro-photographs in photogravure. We doubt if so fine a series of photographs has ever appeared in neurological, or indeed in the whole of medical literature. Whatever further light research may ultimately throw upon the conditions they illustrate and describe, this monograph with its photographs will remain a classic in the literature of the subject. The Vogts recognize eight different types of pathological reaction on the part of the corpus striatum, though the varieties of disease processes from which they arise are much more numerous. Their latest classification of these is into the following types:

1. **État marbré (status marmoratus).** The characteristic clinical picture associated with this lesion is double athetosis of congenital origin, but they appear to include in their series of eight cases of this type examples to which this label cannot rightly be applied, notably Freund's case, Gustav Scholz, a congenital idiot with spastic paraplegia and inco-ordination, but, according to Freund, who studied the case clinically, no involuntary movements recalling athetosis. Foerster deals with this point in a paper to be referred to later. The lesion is an aggravated form of the 'plaques fibro-myeliniques' which C. Vogt has described as normally present in the cerebral cortex, situated in the striatum (nucleus caudatu + putamen). The pallidum (globus pallidus) is relatively intact. The lesion consists in distinct and thickly scattered areas in which ganglion cells are absent, and appear to be replaced by a network of fine nerve-fibres. In Weigert specimens the condition gives the striatum a mottled appearance, hence the name état marbré. In addition, there is a secondary degeneration of strio-pallidal nerve-fibres. They regard the condition as a developmental defect.

2. **Stationary état fibreux (status fibrosus).** One case is described. In this the primary lesion was an encephalitis in childhood leading to atrophy of one cerebral hemisphere. The striatum lesion was a selective nerve-cell necrosis involving the small association cells of the striatum and their fine processes. This resulted in a shrinkage of the caudate and putamen and an abnormal approximation of the persisting nerve-fibres, which gives the tissue an unduly fibrous appearance in Weigert specimens. The symptomatology included epileptiform attacks, spastic hemiparesis, and athetosis, the last mentioned being the striatum component.

3. **Progressive status fibrosus.** (*a*) A pure striatum lesion of the type described above occurring in non-hereditary chronic progressive chorea. (*b*) Associated with cortical changes in Huntington's chorea, the cortical lesions being the basis of the mental symptoms. The aetiology of both types is unknown. (*c*) As part of the disease process in rare cases of general paralysis of the insane. The aetiology in these three types is different, but the tissue reaction is identical. It does not appear that the lesion is altogether confined to the striatum, for a similar but less intense change is sometimes noted in the pallidum.

4. **État dysmyélinique (status dysmyelinatus).** Appears clinically as a bilateral athetosis passing ultimately into a generalized muscular rigidity. Two cases are described. The lesion begins in infancy and consists in a progressive loss of the nerve-fibres of the striate system, strio-pallidal and pallido-fugal, especially the latter.

5. **Total necrosis of the striatum.** The case they describe is one of torsion dystonia, or torsion spasm, which Thomalla has already reported. To this group, according to the authors, belongs Wilson's progressive lenticular degeneration with hepatic cirrhosis, and also the ' pseudosclerosis ' of German authors. The lesion begins in the putamen, spreading to the caudate and later to the pallidum. They give torsion spasm as the characteristic clinical picture, but in Wilson's cases generalized rigidity and tremor was constant, without involuntary movements of other forms.

6. **Foci of neuroglial proliferation in the striatum with pre-senile changes in the striate system.** A single case is described. The symptom complex included torsion spasm, athetosis, and rigidity of paralysis agitans type. There was hyaline and calcareous degeneration of the vessels of the brain, round-celled infiltration of the cortex and of the vessels of the corpus striatum. The perivascular spaces here were widened and the caudate shrunken. The putamen and pallidum were less seriously involved. In the striatum there were some areas of nerve-cell degeneration with neuroglial proliferation.

7. **État de désintegration (status disintegrationis).** The clinical picture is that of paralysis agitans without tremor when the lesion is confined to the pallidum, but with striatum involvement tremor also makes its appearance. The lesion includes gross atrophy of the caudate from loss of both cells and fibres, small lacunae from haemorrhage and thrombosis, with rarefaction and absorption of tissue round the vessels. The last-named leads to the ' état criblé ' when small vessels are concerned and to the ' état lacunaire ' in the case of the larger vessels. The condition corresponds to Pierre Marie's ' état lacunaire de désintégration '.

8. **Gross vascular lesions of the corpus striatum.** A single case is described—one of arteriosclerosis with a softening of the striatum on one side. The patient was a dement with hemiathetosis.

In their analysis of the syndromes of the corpus striatum, the authors point out that the corpus striatum as a whole includes centres of different physiological rank and function. The striatum is the more recently developed and the more highly specialized structure, the pallidum being older phylogenetically and of lower rank. In this connexion a brief reference to a paper of Elliot-Smith's on this aspect of the subject may be germane. He believes that the striatum (nucleus caudatus and putamen) is hypopallial in origin, that is, it arises from the primitive pallium by a turning in of cells on the lateral aspect of the pallium to form a cap to the palaeostriatum, which latter forms a thickening on the floor of the lateral ventricle. These cells come ultimately to form the caudate, putamen, and claustrum. The lateral striate artery enters the brain in association with this pallial formation, and comes in man to be the lenticulo-striate artery, 'the artery of cerebral haemorrhage'. In short, the striatum (caudate + putamen) is cortical in origin. From these facts, C. and O. Vogt conclude that loss of striate activities results in involuntary movements, which are due to 'released' and uncontrolled pallidal function. Loss of pallidal function, on the other hand, produces generalized rigidity, the effect of 'release' of sub-pallidal motor centres. Unilateral lesions of the pallidum, however, give rise to the striatum syndrome owing to the bilateral connexions of the pallidum. The presence of a lesion of the cortico-spinal or pyramidal system masks the symptoms of lesions of the corpus striatum. Their physiological conclusions may be summarized as follows: (i) The corpus striatum (striatum + pallidum) of apes and of man is identical in structure and in physiological value. (ii) There is a period after birth, before the striatum system is myelinated, when the pallidum functions are uncontrolled, and the diffuse motor activities of the new-born infant are pallidal reflex reactions. (iii) Motor impulses travelling *via* the cortico-spinal system do not make connexion with the striate system of fibres, which (iv) receives its afferent impulses through the thalamus. (v) The striatum is a controlling organ superimposed anatomically and physiologically upon the pallidum, whose simple activities it not only controls but also refines. This control is involuntary and 'automatic'. Further, the striatum is the organ for the execution of associated and emotional movements, postural reactions, and flight and defence reactions. The motor defects in voluntary movement from lesions of the striatum indicate that these activities are embodied in the voluntary motor activities mediated by the cortico-spinal system. (vi) The pallidum is the centre for many primitive movement complexes. The movements of the new-born infant are manifestations of its activity. Further, it controls sub-pallidal centres, and the rigidity of paralysis agitans is the expression of the activity of these centres. Tremor is the result of minimal grades of striatum defect. More severe defect results in the appearance of athetosis, when the lesion occurs in early life, and in choreiform movements when disease occurs in adult life. Each of the components of the striatum and pallidum syndromes is analysed at some length on these lines.

A detailed analysis of the clinical and pathological basis of these conclusions is impossible within the scope of this short notice, but the doubt may be expressed whether the lesions are sufficiently pure, or the symptom-complexes sufficiently constant and clear-cut, to justify the attractive simplicity of the authors' classifications, while the physiological conclusions lie under the same uncertainty. Elsewhere (cf. *Medical Science*, 1922, **6**,

46) Pierre Marie has pointed out that he has examined hundreds of cases of the 'état lacunaire' in which, during life, any variety of corpus striatum syndrome had been conspicuously absent. Further, the variety of symptoms which appear to follow the lesion classified as 'total necrosis of the striatum', ranging from the extravagant contortions of torsion spasm to the rigidity and tremor of Wilson's disease, seems to indicate that the rigid separation of striatum and pallidum syndromes is, to say the least, premature. C. and O. Vogt suggest that the decerebrate rigidity of Sherrington may be a sub-pallidal release symptom. But, as Magnus has recorded, removal of the hemispheres, including the corpora striata in cats or dogs, does not produce either decerebrate rigidity or loss of reflex movements of associated and emotional (pseudaffective) type. To produce decerebrate rigidity the anterior portion of the mid-brain must also be removed, and the rigidity resulting does not resemble the generalized rigidity of paralysis agitans, but is identical with the spasticity of pyramidal tract lesions.

In short, the physiological conclusions concerning the corpus striatum reached by the authors, and by others on a clinico-pathological basis cannot at present be brought into line with the results of experimental physiology; indeed these conclusions would probably never have been formulated had their authors acquainted themselves with the knowledge derived from the experimental physiology of the nervous system during the past twenty-five years.

Foerster's paper is a detailed analysis of striate syndromes on a clinical basis. He gives the following purely clinical classification: (1) Chorea. (2) Paralysis agitans. (3) Arteriosclerotic muscular rigidity. (4) Pseudosclerosis and progressive lenticular degeneration. (5) Athetosis. (6) Torsion spasm (cf. *Medical Science*, 1920, **2**, 67). (7) Spasmodic torticollis. (8) Myoclonus. To these the Vogts would add Little's disease, but Foerster does not accept its unqualified admission, and we believe rightly, because, as he points out, the term has been used to comprehend several distinct clinical and pathological conditions. These he classifies as follows: (*a*) Congenital spastic paralysis of pure pyramidal type. (*b*) A rare form showing rigidity of pallidal type. (*c*) Congenital double athetosis, occurring in premature children. (*d*) Combined pyramidal and pallidal forms.

Foerster considers the corpus striatum syndromes under two main headings, the syndrome of the striatum and that of the pallidum Paralysis agitans he accepts as the typical clinical counterpart of pallidal lesions, but he adds the arteriosclerotic muscular, which he himself has described, and also the Parkinsonian syndrome which may follow encephalitis lethargica.

He gives a minutely detailed description of all the symptoms of **the pallidal complex**, which may be summarized as follows:

1. Tremor at rest.
2. Increased plastic muscle tone.
3. Increased resistance to passive stretching of the rigid muscles.
4. What may be called a 'shortening reaction' (Adaptationsspannung) on approximating the insertions of a muscle.
5. Tonic persistence of contraction on electrical stimulation.
6. Absence of all the reflex reactions characteristic of pyramidal tract lesions.
7. No expressional or reactive (Reaktiv-) movements. By the latter is apparently intended postural reactions to movement.

8. Limitation of voluntary movements ('Bewegungsarmut'). This includes, as component factors, slowness in initiating and completing movement, diminished range of movement, diminished force of movement, and tonic persistence of movement.

9. Loss of normal associated movements.

In his physiological analysis of this syndrome, Foerster gives a detailed account of the fibre connexions of the pallidum according to the Vogts, and accepts the view, also put forward by Kinnier Wilson, that there is no direct cortico-pallidal path. He regards the pallidum as an intermediate station in a cortico-muscular efferent path, and as the efferent organ of the thalamus. The pallido-fugal fibres also enter into other physiological systems, notably, according to Foerster, in the proprioceptive cerebellar system. The syndrome includes **defect** and **release** symptoms. Among the former are loss of emotional and associated movements and postures, the slowness, the weakness, and the diminished excursion of voluntary movement. These are due to interruption of a cortico-thalamo-pallido-muscular path for voluntary motor impulses. The pallidum is concerned in the voluntary carrying out of the associated movements which normally accompany isolated purposive movements, the latter employing the pyramidal path. It is also concerned with movements of expression. Hence both are abolished in the pallidal syndrome. The release symptoms include the tremor, the rigidity, the fixation of postures, and the anomalies of attitude. The second and third of these are reflex phenomena of proprioceptive type, according to the author, and he makes the interesting statement that **posterior root section** abolishes them, as does also a supervening tabetic process. This is a very important point, and we believe that it is the chief merit of the author to have pointed this out, for knowledge on this matter is clearly an essential preliminary to any scientific study of pallidal rigidity. He believes that normally the pallidum exerts an inhibitory action on the cerebellar proprioceptive system, and it is the removal of this influence which allows an uncontrolled over-action of the cerebellum with a resulting muscular rigidity. A similar explanation is advanced to account for the tremor. In short, the pallidum carries out associated and emotional movements and inhibits the activity of the cerebellar system.

The striatal or athetotic syndrome. Congenital double athetosis is the typical example of this. Foerster gives a detailed description of the component symptoms, which he classifies as follows: (1) Athetosis at rest. (2) Muscular atonia in the intervals between the mobile spasm. (3) A characteristic attitude ('Hockerstellung'). (4) Undue extensibility of the muscles. (5) Inconstant and variable fixation spasm. (6) Excessive emotional and reactive movements (postural reactions). (7) In any movement, the antagonists, instead of being reciprocally inhibited, go into even stronger contraction than the prime movers, and, in addition, innervation spreads abnormally to other muscle groups. As a result, a single circumscribed movement becomes impossible, and widespread athetotic disorder is added to each attempt. He points out that 2, 4, 6, 7 are directly opposite to certain components of the pallidal syndrome.

Foerster agrees with the Vogts in their classification of symptoms into striatum and pallidum syndromes on a pathological-anatomical basis, but whereas the latter compare the movements of athetosis with the diffuse movements of the new-born child, Foerster believes that they resemble the normal motor activities of climbing apes. He analyses this supposed

resemblance in some detail, and believes, that in lesions of the striatum in man, the previously inhibited primitive ape-like synergies of the pallidum run riot owing to 'release'. He believes the striatum, on the other hand, to have specifically human functions. A difficulty then arises in explaining why apes which possess a striatum should climb and leap as their normal mode of movement, and he seeks to explain this by supposing that such a structure as the striatum may not begin to function in the animal type in which it first makes its appearance. Therefore, the striatum having developed in the common ancestor of apes and man, has remained functionless in modern apes, and has taken over its specific functions in man alone. Earnestly as these hypotheses are advanced by their author, it is impossible to take them seriously. His views as to the inactivity of the simian striatum are without any basis whatever, while how the exquisitely co-ordinated motor activities of the climbing monkeys can be compared with the incoordinate writhings of the tormented musculature in a case of athetosis will be beyond the comprehension of any one who has ever delighted in watching the amazing agility of the inhabitants of a monkey-house.

In describing the symptom-complex of **chorea**, the chief points of difference emphasized by Foerster are the rapidity of the involuntary movements and the absence of any 'braking' effect from concurrent contraction of antagonists. This he attributes to a simultaneous involvement of the cerebellar system, which results in atonia.

Throughout Foerster's physiological analysis of the various components of these syndromes, we find great stress laid upon an infinitely precise localization of function within certain anatomically recognized and described nuclei and fibre systems. In this way paths and circuits of extreme complexity are composed, but throughout the whole exposition there is no convincing physiological conception of the functions thus localized. Those fundamentally important aspects of nervous system physiology which have been so frequently emphasized in this journal appear to be a closed book to the author, and for the most part he is trying to localize he knows not what. Nevertheless, in spite of the freedom with which we have felt compelled to criticize Foerster's theoretical expositions, we cannot but admire the minuteness and lucidity of his clinical descriptions, which are clearly the fruit of an exceptional experience. In this respect alone the paper merits close study. Its pages are illustrated by a unique series of 173 excellent photographs.

In his short paper on the histology of paralysis agitans and Huntington's chorea, Lewy deprecates what he considers the somewhat unduly precise notions of the Vogts. In a previously recorded series of observations on the brains of twenty cases of paralysis agitans, he did not find the lesions exclusively limited to the striate system. He believes that careful cytological studies of cases of the kind examined by the Vogts would reveal a less simple state of affairs than their studies by the Weigert method have indicated. In cases of chronic chorea, both hereditary and otherwise, Lewy finds that both striatum and pallidum are markedly shrunken, pale, and not clearly marked off from each other. The cell lesions are extreme and primary in both organs. He describes in some detail the nerve-cell changes in paralysis agitans and chronic chorea. In the former there is a general atrophy of the large cells of the pallidum. In chronic chorea, the smaller nerve-cells of the striatum are severely damaged, but so are the pallidal cells. He has also found similar changes in the cells of the cortex and in

those of the cerebellum. On the whole, however, he agrees that in paralysis agitans the pallidum is predominantly involved, and in athetosis and chorea, the striatum.

The impression derived from these three studies is that a wealth of exact information as to the symptomatology and pathological anatomy of diseases of the corpus striatum is being acquired, but that knowledge is not yet ripe for a conclusive analysis or interpretation of this. Such attempts at physiological analysis as are contained in these papers are extremely speculative, and, as we have indicated, they are like so many attempts of the kind within recent years not based upon modern physiological ideas. Without exception they ignore all that we have learned of the co-ordination of movement and posture from experimental physiology in the past twenty years, and they continually invoke the most far-fetched phylogenetic considerations. In the circumstances, it is difficult to take an optimistic view of their value. Nevertheless, the labours of these and other workers in this fascinating field are yielding information of the greatest value for all students of the problem.

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Foerster, O. Zur Analyse und Pathophysiologie der striären Bewegungsstörungen. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **73**, 1.

Lewy, F. H. Zur pathologisch-anatomischen Differentialdiagnose der Paralysis agitans und der Huntingtonschen Chorea. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1921, **73**, 170.

Vogt, C. Quelques considérations générales à propos du syndrôme du corps strié. *J. f. Psychol. u. Neurol.*, 1911, **18**, Ergänzungsheft 4, 479.

Vogt, C. u. O. (1). Erster Versuch einer pathologisch-anatomischen Einteilung striärer Motilitätsstörungen nebst Bemerkungen über seine allgemeine wissenschaftliche Bedeutung. *J. f. Psychol. u. Neurol.*, 1918, **24**, 1.

Vogt, C. u. O. (2). Zur Kenntnis der pathologischen Veränderungen des Striatum und des Pallidum und zur Pathophysiologie der dabei auftretenden Krankheitserscheinungen. *Sitzungsberichte der Heidelberger Akademie der Wissenschaften, Abteilung* B, *Biologische Wissenschaften*, 1919, 14. Abhandlung.

Vogt, C. u. O. (3). Zur Lehre der Erkrankungen des striären Systems. *J. f. Psychol. u. Neurol.*, 1920, **25**, 631.

F. M. R. W.

ABSTRACTS

SURGERY

Gallie, W. E., and **Le Mesurier, A. B. The use of living sutures.** *Canad. M. Ass. J.*, 1921, **11**, 504.

For some years the authors have been experimenting with the use of autogenous transplants of tendon and fascia for the purpose of filling gaps in tendons and for repairing herniae and other defects. They found that such implants lived well. Experimentally they excised patches of fascia in rabbits and immediately stitched them back in place with black silk threads. During the first few weeks the specimens showed ordinary phenomena of inflammation, but after the third week these phenomena gradually subsided and there was nothing to indicate that the cells or fibres had been changed in any way or that their physiological value had been altered. In a second series of experiments they found that muscular aponeurosis transplants behaved in the same way, whilst in the third series similar results were obtained with tendons. They found that if it were necessary to use thick transplants of tendon it was advisable to split them longitudinally into several strands in order to allow free permeation of lymph to the deeper parts. In neither fascia, aponeurosis, nor tendon was there any multiplication of the ordinary cells of the tissue; healing occurred by ordinary scar tissue, and therefore the joins were capable of stretching; hence the clinical and practical value of the method was diminished. To overcome this defect they have adopted the plan of weaving narrow strips of transplant through slits made in the fasciae of the surrounding tissues, or in other words 'darning' the hole. This plan, especially if the strips be fixed by suture and all knots in them similarly fastened by some sutures, they have found very efficacious. It is important that the fascial strip shall be free of the fat and areolar tissue that normally ensheaths it if strong union is to be obtained rather than a stretchable scar tissue. They have used these methods in the repair of tendons and ligaments—for example, in recurring lateral dislocation of patella, in recurring dislocation of the shoulder, in bridging gaps in tendons, in the treatment of congenital ptosis, and in herniae. Since the date of this publication they have done more work, and propose to publish further shortly. C. C. C.

Matthieu, P. Rupture de la vessie par fracture du pubis. [**Rupture of the bladder by a fracture of the pubis.**] *Bull. et mém. Soc. de chir. de Par.*, 1921, **47**, 870.

The case was one of a drayman upon whom a boiler-lid fell from his cart. He afterwards walked about 20 yards and then felt an uneasy sensation in the lower abdomen. A short time later he was brought to

hospital and was found to have an anterior dislocation of the right shoulder and a few drops of blood escaping from his urinary meatus; he had no desire to pass urine. Two hours later there was general abdominal rigidity, the pubic region was very painful and a catheter passed into the bladder drew off nearly pure blood. A median sub-umbilical incision was made and the absence of any intraperitoneal injury established. A large prevesical extravasation was seen. The peritoneum was completely closed and a suprapubic incision made. After sponging away a mixture of blood and urine a median cystotomy was done with some difficulty, and it was then seen that the right lateral wall of the bladder was perforated by a bony point arising from the fractured pubis. This point was pushed back into place with the finger and the perforation closed with catgut. Suprapubic drainage was established and the dislocation of the shoulder reduced. The patient recovered. F. J. F. B.

Leighton, W. E. Spontaneous rupture of the malarial spleen with an abstract of cases reported between 1842 and 1921. *Ann. Surg.*, 1921, **73**, 13.

A spontaneous rupture of the spleen which has been enlarged owing to malaria is relatively uncommon. The author reports in detail a case of spontaneous rupture in a white male, aged 35. The lesion was satisfactorily treated by operation and two parallel rents were found on the external surface of the spleen. Haemorrhage was controlled by gauze packing and the patient recovered.

Seventy-two other cases are abstracted from the literature. He says the treatment is essentially surgical and very frequently the spleen must be removed. In the reported cases of operations the mortality was 12·44 per cent. A. J. W.

Eccles, W. McAdam, and **Freer, G. D. Enlargement of a spleniculus to the size of a normal spleen.** *Brit. M. J.*, 1921, ii, 515.

In this contribution a detailed account is given of a man, aged 21, whose spleen was removed for a rupture in Kuala Lumpur on May 24, 1910. Convincing evidence is brought forward that it was actually the spleen that was removed and there are notes to say that it was of nearly double the normal size owing to the patient having had malaria. He later returned to England and sought advice on account of a large ventral hernia which had occurred in the scar of the original wound.

On September 4, 1920, he was operated upon by Mr. Eccles, who was assisted by Mr. Girling Ball. On opening the abdomen a spleen which was of the normal shape and appearance was seen in the usual position and because of the knowledge of the past history its size, shape, and relationships were very carefully investigated. The normal left kidney was palpated so as to eliminate the possibility of the mass being an abnormally placed kidney. The condition was regarded as a splenculus which had enlarged to the size of a normal spleen. A. J. W.

Speese, J., and **Brown, H. P. The malignant degeneration of benign tumours of the thyroid gland.** *Ann. Surg.*, 1921, **74**, 684.

Although it is generally admitted that cancer of the thyroid gland has a tendency to develop on pre-existing disease, experience differs as to the

frequency of this degeneration. The authors point out that in Pennsylvania the percentage was 4·6 as compared with a 1·6 per cent. found by Balfour.

In laying stress upon the fact that there is generally some primary benign lesion they point out that some of the carcinomata are of such slow growth that it is possible that some of these cases were carcinomatous from the beginning. It is probable that the changes in old adenomata act as a chronic irritant and that in many such cases the epithelium may be so atypical that it is difficult to distinguish from carcinoma.

Their own investigation is based upon 426 lesions of the thyroid gland in which cancer occurred 19 times and sarcoma three times, but in addition to this group there were 6 cancer cases from outside sources, giving a total of 28 malignant thyroid tumours. In 5 of these cases the predisposing history of a simple goitre could not be obtained, but it was quite definite in the remaining 78·5 per cent. The average time at which the benign tumour had existed before the onset of carcinoma was 12·6 years. There were toxic manifestations of tremor, tachycardia, and loss of weight in 5 cases. As a general rule the onset of carcinoma is indicated by enlargement and increased consistency of the growth, but a radiating and neuralgic pain was the first symptom in 5 cases, and the onset of dyspnoea also in 5 cases. They lay stress upon the difficulty of diagnosis in the early stages and state that the majority of their cases were only discovered after operation. These naturally are those which give the best prognosis, and the 8 cases in which there was no record of recurrence all belong to this group. In such varieties the prognosis is fairly good, and complete extirpation of the thyroid is not necessary if the malignancy is limited to an adenomatous nodule and has not extended beyond the capsule of the gland.

In discussing the aetiology they point out that carcinoma rarely involves the entire gland for it usually commences in an adenomatous nodule, and for a considerable time is limited to one lobe. The progress is very variable. In those occurring secondary to an adenoma the course is slow and sub-acute. In the rarer type, where the disease is primary, there is usually at first a slow-growing localized nodule which suddenly becomes active and infiltrates the thyroid and the surrounding part. At the other extreme is seen a variety which is described as the acute type, where there is a sudden increase in size followed by a rapid invasion of the surrounding parts. It is often fatal in a few weeks and is usually seen in comparatively young people.

The authors lay stress upon the necessity, in the treatment of all goitres, of freely exposing both lobes, so that a small adenomatous nodule, from which malignancy may later develop, may not be overlooked. When carcinoma is clinically definite the prognosis from operation is poor. A. J. W.

Gillett, A. S., and **Wakeley, C. P. G. Selenium in the treatment of malignant disease.** *Brit. J. Surg.*, 1922, **9**, 532–9.

In view of the conflicting reports of cases of treatment of malignant disease with selenium during the last ten years, Gillett and Wakeley have investigated its action in over 100 cases. The question of dosage became an urgent one early in their investigations, and they found that persistence with a large dose (5 c.cm.) every week led to disaster and excessive reaction; in most cases a smaller dose should be given immediately after the maximum had been reached. Leucocytosis followed the earlier doses, but not the later

ones in a given case; no other blood changes were found; the early leucocytosis may account for apparent improvement at the beginning of the course of treatment. After the earlier doses general toxaemia was improved, but later the opposite occurred, and toxaemia, necrosis, ulceration, and secondary haemorrhage increased. The selenium was given intramuscularly. Of the first 50 cases treated by them all died without apparent prolongation of life; of the second 50, 30 have died, 10 are in a dying condition, and 10 are alive; but of these 10 6 are cases of atrophic scirrhous cancer of the breast. They conclude that temporary improvement only can be expected; that small doses are essential, the number of injections being limited to 8 or 10; that pain and insomnia are aggravated in most cases; that they never saw the gain in weight noticed by other observers. C. C. C.

Bertocchi, A. Contributo allo studio dell' ' angioma arterioso racemoso '. [**Contribution to the study of racemose arterial angeioma.**] *Arch. ital. di chir.*, 1922, **5**, 63–85.

A careful histological examination of the structure of a racemose angioma, occurring in a man of 37 as the result of a severe trauma at the site of a small telangioma of the forehead.

The author reviews the various opinions advanced as to the true nature of these tumours, and, notwithstanding his derivation of his own, and some 12 per cent. of all similar tumours from ' trauma ', upholds the view that they are true neoplasms. He bases his conclusion on the observation that the adipose tissue at the periphery of the mass shows multiple vessels of new formation with gradual transformation into angiomatous tissue. He observes in all vessels, on the arterial side, transformation of the tissues of the various coats, which, notwithstanding periods of hypertrophy and multiplication of cells, tend to eventuate in disappearance of the muscular and elastic elements; in connective tissue substitution; and final hyaline degeneration, at any rate of the intima, in which proliferation frequently proceeds to complete obliteration of the lumen. The veins, though dilated and exhibiting evidence of changes analogous to those met with in aneurysmal varix, and though contributing to the mass and the pulsatility of the tumour, are not to be regarded as sharing in the neoplasm proper.

E. R. C.

Key, E. Embolectomie als Behandlungsmethode bei embolischen Zirkulationsstörungen der Extremitäten. [**The treatment of embolic disturbances of the circulation in the limbs by embolectomy.**] *Acta Chir. Scand.*, 1922, **54**, 339.

Key reviews the 45 cases (8 being his own) in which 48 operations for removal of an embolus in an artery were performed. In no fewer than 20 cases disease of the mitral valve was diagnosed. The sex distribution was fairly even, the ratio of males to females being 24 to 21. The youngest patient was a boy of 12, the oldest a woman of 72. In 22 cases the operation was performed for embolism of the common femoral artery. In Key's first case (1912) the interval between the embolism and the operation was 7 hours; the restoration of the circulation in the toes was slow, and a peroneus paresis persisted for a long time. He was, therefore, inclined to think that 7 hours was about the outside limit of delay if the operation was to be successful. Since then this interval has been successfully extended, by Lundmark to 10 hours, by Sundberg to 12, by Widerõe to 14, by

Pupovac to 16, and in his last case (1921) by Key himself to 22½ hours. A classification of the cases according to the length of the interval between embolism and operation showed the importance of early operation; in 39 cases the length of this interval has been published, and it varied from 1½ hours to 28 days. In 23 cases, in 13 of which the operation was successful, it was performed within 24 hours of the embolism. Of the 12 cases operated on within the first 10 hours, 9 were successful, whereas of the 5 cases operated on after an interval of 11 to 15 hours, only 2 were successful. Of the 7 cases operated on 16 to 24 hours after the embolism, only 2 were perfectly successful; one of these successes was achieved by Key in his last case. He concludes that after an interval of 10 hours the prognosis rapidly becomes worse with delay. With regard to the ultimate results, he points out that, as in most cases the heart is diseased, the successful results of embolectomy are apt soon to be stultified by further progress of the primary lesion. Many patients have, however, lived in comparative health for several years after the operation and have been able to lead a fairly active life. Key discusses at considerable length the technique of the operation, its indications and prognosis, and, in addition to his detailed account of his own cases, he summarizes seriatim those of other surgeons.

C. L.

Bull, P. What can more than 6,000 post-mortem examinations teach us about emboli and embolic gangrene of the extremities? *Acta Chir. Scand.*, 1922, **54**, 315.

Among 6,140 necropsies made between 1895 and 1920 Bull found 15 cases of embolism in the limbs, 6 being followed by gangrene. In 13 cases thrombi were found in one or more of the cavities of the heart and in the 2 remaining cases the primary thrombosis was presumably situated in the aorta. In 243 cases, i. e. in 4 per cent., thrombosis was found in the arteries (e. g. the aorta) and the heart, and in 73 of these cases thrombotic deposits were observed on the valves of the heart. In the majority of these cases of cardiac thrombosis, pathological changes were found in the heart itself, and in no fewer than 48 cases pathological changes were also found in the kidneys. In 6 cases of thrombosis in the heart the patient's age ranged from 7 months to 13 years, and the age of the oldest patient was 86 years. Thus there is no absolute age limit for this condition, and embolic gangrene of the limbs may occur at any age. The practical significance of this finding is that gangrene of the limbs in old people is not necessarily senile gangrene. When the symptoms appear suddenly and on one side only, and gangrene occurs after a short interval above the ankle or still higher up the leg, embolic gangrene should be suspected irrespective of the patient's age. Only in 1 of the 15 cases was it not possible to prove the existence of embolism in other organs; in the remaining 14 cases, 30 emboli in other organs were found. Bull's main conclusion is that embolism of the limbs should not be regarded as an isolated phenomenon, but merely as a link in a chain of emboli in other organs.

C. L.

Bernheim, B. M. Blood transfusion. *J. Am. M. Ass.*, 1921, **77**, 275–7.

Bernheim calls attention to the dangers attending citrate transfusion, namely, the certainty of a reaction more or less severe in a considerable proportion of cases. He defines as groups for which this method of

transfusion must not be employed (1) those cases in which shock is already so profound that additional shock might be fatal and (2) those in which profound exsanguination has occurred. The subsequent discussion did not result in any definite views as to the cause of these reactions, but Lewisohn is investigating the possibility that chilling of the blood is responsible.

G. W.

Cheinisse, L. De la transfusion au citrate. [**Transfusion with citrated blood.**] *Presse méd.*, 1922, **30**, 171–2.

Unger, L. J. The deleterious effect of sodium citrate employed in blood transfusion. *J. Am. M. Ass.*, 1922, **78**, 2107–9.

Hartman, F. W. Transfusion reactions and citration within the needle. *J. Am. M. Ass.*, 1922, **78**, 15–18.

Ravdin, I. S., and **Glenn, E. The transfusion of blood with report of 186 transfusions.** *Am. J. M. Sci.*, 1921, **161**, 705–22.

Cheinisse discusses the indications for citrate and whole blood transfusion, his article being in the nature of a review of recent literature on the subject. He concludes that the citrate method has certain dangers owing to the action of citrates on the red cells and that to this extent the method can never be that of choice if whole blood is available. But when there are insuperable obstacles to the employment of whole blood, the citrate method remains an important addition to the resources of the therapist.

Unger, discussing the same subject, states, as the result of clinical experience and experiment, that sodium citrate increases the fragility of red cells and diminishes the amount of complement. Further, it 'practically destroys the phagocytic power of white blood cells'. He advocates the choice for whole blood transfusion of blood with a high phagocytic index, particularly when the control of sepsis is in question.

Hartman finds that some at least of the bad results of citrate transfusion are due to coagulation within the needle or tubing which conveys the blood from the vein to the citrate. He has accordingly worked out an apparatus for citrating the blood in the needle as it leaves the vein, and claims that he has reduced reactions by 50 per cent.

Ravdin and Glenn give first an historical review of blood transfusion. This is followed by an account of their own cases and then by a detailed consideration of this material together with that afforded by 117 papers by other authors to which references are given. Their conclusions are therefore of more than usual interest and are as follows: (1) With the element of risk practically eliminated, blood transfusion has become one of the most effective procedures in modern therapeutics. The authors, however, have lost three cases in which the blood had been carefully tested, but all were very severe cases of pernicious anaemia. (2) Transfusion is a specific in acute haemorrhage where the limit of bleeding has not been reached, in melaena (neonatorum), and in the haemorrhage of haemophilia. The authors consider that there is too much hesitation in resorting to transfusion in acute haemorrhage. (3) It is of definite value in primary pernicious anaemia in hastening and prolonging remissions. It is indicated in cases of severe secondary anaemia. After transfusion, operations on debilitated or anaemic individuals may often be safely undertaken that otherwise would involve serious risk. (4) Transfusion in shock is not as efficacious as in shock associated with

haemorrhage. (5) They have not been able to prove the value of transfusion in acute infections, but in chronic infections they have had results justifying its use. (6) Transfusion is of unproved value in acute leukaemia. In aplastic anaemia it is at the most a temporizing procedure. (7) The difference, as far as reactions are concerned, between the citrate method and the Kimpton-Brown method is practically nil, and the simplicity of the former warrants its preference. G. W.

Runeberg, B. De hematogena, akut infektiösa nefriterna och pyelonefriterna. [**The hematogenous, acutely infectious nephritides and pyelonephritides.**] *Finska Läk-sällsk. Handl.*, 1921, **63**, 473–92.

The material with which Runeberg deals consists of about 250 cases of renal disease, the origin of which was 'spontaneous'. In nearly all these cases there was no history of disease of the urinary tract. However divergent opinions may be as to the aetiology of these cases, the frequency with which they occur is undeniable; they represented more than 50 per cent. of all the cases of acute disease of the urinary tract admitted to Professor Runeberg's surgical wards in Helsingfors in the period 1914–20. In not one of these cases was simple acute cystitis the precursor of the renal disease, and whenever acute cystitis was found associated with normal micturition and an intact urethra the renal system was also already involved. The cystoscope frequently showed the bladder to be intact even in the face of symptoms of intense cystitis; still oftener it showed, indeed, cystitis, but this was invariably combined with ureteritis and pyelonephritis. Hence Runeberg's conclusion that all these cases of 'spontaneous' acute diseases of the urinary tract are due to hematogenous infection of the kidneys, which he regards as the main portal of exit for germs circulating in the blood. Again and again, in apparently localized inflammatory conditions such as osteomyelitis, phlegmons, carbuncles, and the like, he has succeeded in demonstrating bacteria in the urine, and he has often noticed that the surgical cases just referred to have presented signs pointing to involvement of the kidneys, such as slight haematuria or albuminuria with a few bacteria in the urine, or other more serious manifestations of renal disease. In 40 cases in which nephrectomy was performed he has investigated the lesions microscopically, and he has found many points of difference, clinical and other, between the coliform and the staphylococcal infections. The coli infections, even when the pyelonephritis seemed to be far advanced, showed a remarkable tendency to spontaneous healing; in a few weeks or months most alarming symptoms would vanish. In some cases the disease would clear up completely, no evidence being left except the persistence of bacteria in the urine. Frequently, however, relapses occurred. While with coli infections pus and every sign of disease except bacteriuria might vanish, the reverse was sometimes observed with staphylococcal infections, the germs disappearing from the urine although severe pyuria persisted. In about 80 per cent. of the coli infections and only in 20 per cent. of the staphylococcal infections the patients were females. To ascertain whether improvement in the condition of the bladder and of the kidneys occurs simultaneously or not, Runeberg carried out systematic cystoscopic examinations which showed that as a rule the symptoms of cystitis disappeared before catheterization of the ureters showed complete recovery of the kidneys. But occasionally cystitis per-

sisted long after the primary renal disease had healed completely. In this connexion Runeberg ridicules the surgeons who, on the evidence of an occasional cystoscopic examination, conclude that when cystitis is found without pyelonephritis, infection must have arisen from the urethra. Only repeated systematic cystoscopic examinations can throw light on this question.

Runeberg found that, next to the coli infections, aseptic renal pyuria was the most common condition among his patients suffering from 'spontaneous' disease of the urinary tract. In more than half these cases tuberculosis could be excluded, and the common teaching that aseptic renal pyuria is indicative of tuberculosis and is an indication for operative treatment should be rejected. These cases probably represent a late stage of a staphylococcal infection by the blood-stream. With regard to treatment, the view that cystitis is always secondary to hematogenous renal infection suggests that the practice of irrigating the bladder is futile, at any rate in early phases of the disease. In the later phases it may prove beneficial. The marked tendency towards spontaneous recovery should give the operating surgeon pause; there are, however, certain cases for which nephrectomy is the best treatment, all the more because the disease is often unilateral. A valuable measure is the use of a permanent catheter in the ureter. Particularly in acute cases of pyelonephritis with signs of retention due, probably, to a spasmodic paresis of the ureter, is the drainage effected by a catheter lying in the ureter likely to give relief. C. L.

Runeberg, B. Über die sogenannten aseptischen renalen Pyurien. [**Concerning the so-called aseptic renal pyuriae.**] *Acta Chir. Scand.*, 1921, **54**, 55–89.

Runeberg's paper is an amplification of an earlier paper (*Medical Science*, 1920, **3**, 166) in which he criticized the tendency to regard all cases of so-called aseptic renal pyuria as tuberculous. Many cases in this class are, indeed, tuberculous; but a considerable proportion belong to a totally different category, a distinctive feature of which is the frequent occurrence of congenital malformations of the kidneys. They are, in fact, congenitally defective, and this defectiveness leads in many cases to their becoming the seat of non-tuberculous inflammatory processes. Though the urine may be sterile, it is doubtful whether this sterility is continuous. At any rate microscopic examination of sections of a kidney sometimes reveals micro-organisms, and it is, therefore, probable that they are periodically discharged in the urine. Not infrequently these micro-organisms are staphylococci. In as many as 17 per cent. of the 23 male patients in this category there were definite signs of prostatitis. But it is doubtful whether inflammation of the prostate was of more than secondary importance. This doubt is substantiated by the fact that in two cases in which nephrectomy was performed prostatitis rapidly cleared up after the operation. It is improbable that urinary antiseptics actually provoked aseptic renal pyuria in any of Runeberg's cases, but he regards it as quite probable that when urinary antiseptics are given in sufficient strength to check the growth of bacteria in the urine, they may add to the tale of cases of aseptic pyuria. A negative bacteriological examination of the urine of a patient taking urinary antiseptics should, therefore, be accepted with reserve.

Discussing the differential diagnosis—tuberculous or non-tuberculous

disease—Runeberg emphasizes its difficulty and the many points of similarity. The disease in 72 per cent. of his cases was unilateral, its onset was spontaneous, there were signs of severe cystitis, haematuria was a frequent complication, and the patients were, as a rule, young, pale, and emaciated. The inference that these cases were tuberculous was, therefore, almost unavoidable. But a searching investigation of the case shows many differences in the clinical picture. An acute onset of the disease in renal tuberculosis is the exception, whereas in 60 per cent. of Runeberg's non-tuberculous cases it was acute or sub-acute. And even in the cases in which the onset had been comparatively insidious, the disease had culminated in a few weeks or months. Remissions, which are common also in renal tuberculosis, are more frequent and brief in non-tuberculous cases, severe symptoms and practically symptom-free intervals succeeding each other in the course of a few weeks. The non-tuberculous case often reacts most satisfactorily to a short period of rest in bed, flushing the system with water, urinary antiseptics, and dieting. Equally characteristic is the speed with which relapse occurs if treatment is discontinued too soon. Two other points. Multiple disease of the joints often occurs in these non-tuberculous cases of pyuria, and now and then the demonstration of a primary focus of infection (usually in the skin) gives a hint as to the character of the pyuria.

With regard to the treatment of these cases, even when tuberculosis can be definitely excluded, conservative treatment may have to be abandoned in favour of nephrectomy. When the disease is definitely unilateral and has reduced the patient to severe invalidism, nephrectomy is justifiable, the more so because in many of these cases the kidney is a congenitally imperfect organ. In at least three cases Runeberg performed nephrectomy, although he had convinced himself of the non-tuberculous character of the disease before the operation. C. L.

Rovsing, T. Om kirurgiske Nefriter. [**Concerning surgical nephritis.**] *Hosp.-Tid.*, 1921, **64**, 529–40.

After indulging in a retrospect and a short account of his first nephrolysis in 1892, Rovsing reviews the results he has achieved by nephrolysis or decapsulation in 77 cases of aseptic nephritis. Of his patients 40 were men and 37 were women. With regard to the technique of the operation, an account of which he gives, he removes the capsule of the kidney only when he finds it much thickened and fibrous; otherwise he detaches the capsule from the kidney, but does not remove it. At the operation a piece of renal tissue is removed for microscopic examination, and, as a rule, the ureters are catheterized both before and after the operation. With the data thus obtained, he classifies his material in the following groups: (1) Interstitial nephritis and perinephritis with bouts of pain and haematuria, but without albuminuria between the bouts. All the 26 cases in this group were cured by decapsulation. In most of these cases there were signs of the uric acid and oxalic acid diathesis, and the nephritic and perinephritic changes were probably of a toxic character. (2) Interstitial, usually granular, nephritis with albuminuria, pain, and haematuria. Of the 32 cases in this group, 19 appeared to be completely cured and 9 were much improved by the operation. The remaining 4 patients had died, 2 of them shortly after the operation. In a sub-group, in which Rovsing puts most of his fatalities and short-lived successes, there were 11 cases of advanced,

small granular kidney, some of which were traceable to scarlatinal nephritis. (3) Diffuse parenchymatous nephritis (tubular nephritis, chronic nephrosis). Of the 8 cases in this group, 4 were cured and 2 showed transitory improvement. (4) Glomerular nephritis. Of the 3 cases in this group, 2 were unilateral, and both were cured by decapsulation. Only transitory improvement was effected in the bilateral case. (It should be noted that these cases total 80, whereas elsewhere Rovsing says his total is only 77.)

Rovsing briefly refers to the effect of decapsulation on orthostatic albuminuria. The excellent results usually achieved were probably due to fixation of the kidney in its normal position by the operation. This view is supported by the fact that in most cases the albuminuria can be cured simply by support of the kidney by well-fitting bandages. In his discussion of the rationale of decapsulation, Rovsing records a case in which a remarkable recovery was effected, although at the operation the capsule of the kidney was not tense; it fitted, if anything, more loosely than normal. This case seems, therefore, to give the lie to the hypothesis that recovery depends on relieving the kidney from mechanical pressure. The same case also showed such remarkably rapid improvement that this could hardly have been due to improvement in the circulation due to the development of new blood-vessels and the establishment of new anastomoses. Possibly in this and in other cases decapsulation effected the escape of toxic substances immured between the capsule and the surface of the kidney. Whatever the explanation, this technically easy and, in itself, safe operation should be undertaken in every case of nephrosis which has proved refractory to medical treatment. The fact that the blood-pressure shows a marked fall after the operation, which entails no great loss of blood, is confirmatory evidence of its immediate efficiency. Rovsing concludes: (1) Chronic nephritis is not rarely unilateral. Catheterization of the ureters is, therefore, indicated in the diagnosis of the so-called 'medical' nephritides. (2) Among cases of interstitial nephritis there is a group, characterized by bouts of haematuria and pain, in which decapsulation in the majority of cases leads to complete recovery. (3) Complete recovery or marked improvement can be achieved by decapsulation in cases of parenchymatous and glomerular nephritis, the outlook for which would otherwise be hopeless. (4) There are cases of unilateral, haemorrhagic, parenchymatous nephritis which can be cured by nephrectomy, without which they are hopeless. C. L.

Torraca, L. L'azione di alcune sostanze fotodinamiche sul processo di guarigione delle ferite. [**Influence of certain photodynamic substances in the process of wound-healing.**] *Policlin.*, 1922, **30**, Sez. Chir., 115–27.

There is a group of chemical substances, such as quinine, eosine, acridine, all of them fluorescent, which in the dark are of but slight or no toxicity, but in direct or diffuse sunlight, and in minimal doses, will kill infusoria and cells, and inactivate enzymes and toxines. It is uncertain whether their action is a purely physical one, dependent on the absorption or conversion of rays of given wave-length, or a chemical one resulting from the promotion of oxidation.

To investigate the action of these substances in relation to the inhibition or stimulation of granulation in wounds, the author conducted two series of experiments, with controls, upon guinea-pigs. The one series was

carried out on the Col d'Olen on Monte Rosa (altitude *c.* 9,500 ft.), where the animals were exposed to diffuse sunlight for from 8 to 11 hours a day for 12 days. The other was made in Naples, where the animals were kept entirely in the dark for 12 days. In both cases an area on the back of the animal was shaved and a rectangular wound of known dimensions was made. The effects were recorded as percentages of the original area 'healed'. The substances used, quinine-hydrochloride and methylene-blue, were administered by daily injection. In the dark there was a difference of less than 2 per cent. between the area cicatrized in the controls and that in the animals injected. In those exposed to sunlight definite results were obtained, for whereas with a 0·5 per cent. solution of quinine healing was definitely retarded, with a 0·1 per cent. solution the area epithelialized exceeded by approximately 20 per cent. that in the controls. For methylene-blue the corresponding figures followed precisely the same curve, but were much less striking. E. R. C.

Aaser, P. Pyoctanninum coeruleum (metylviolet) som middel mot suppurerende saar. [**Methyl violet in the treatment of suppurating wounds.**] *Tidsskr. f. d. norske Lægefor.*, 1921, **41**, 817–18.

Aaser has found impetigo contagiosa invariably react promptly and satisfactorily to treatment with methyl violet when a 0·1 to a 1 per cent. solution was applied on a compress. The results were good even when the impetigo had proved refractory to other antiseptic remedies. He has also used a 0·1 per cent. solution with marked success in controlling suppuration in and about the abdominal wound after a prostatectomy. In such cases he paints the wound twice a day with this solution, and then covers the wound with a pad of cotton wool soaked in the same solution. In the above strength this antiseptic is neither painful nor dangerous.

C. L.

Dominici, L. La reazione di Wassermann dopo le cloronarcosi, le eteronarcosi e le rachianestesie. [**The Wassermann reaction after chloroform, ether, and spinal anaesthesia.**] *Policlin.*, 1922, **30**, Sez. Chir., 92–8.

The author considers that the nature of the reaction is not yet established. He regards the possibility of using extracts of other organs than syphilitic liver, and even lecithin and tauro- and glyco-cholate of soda, as throwing doubt on specificity. He cites not only framboesia, but trypanosomiasis, relapsing fever, Weil's disease, malaria, scarlet fever, and even, doubtfully, pulmonary tuberculosis, diabetes, psoriasis, sclerodermia, lupus erythematosus, gout, and eclampsia, as giving, exceptionally at least, a positive reaction. He thinks the reaction cannot be regarded as of the antigen-antibody immunity order. He cites the evidence of Levaditi and Yamonouchi, Porges and Jakobsthal, in favour of a mere quantitative difference in precipitation, and seeks the determining agent in substances liberated by lysis of tissues, pre-eminently by the spirochaete, but also conceivably by many other noxa. He cites the experiments of Bittorf and Sckidorky on the total suppression of haemolysis following mere pulping of the cerebellum; and the affirmation of Kaplan that simple ingestion of alcohol in great quantity will produce a positive W.R. Thence he passes to the suggestion that the known affinity of chloroform and ether for hepatic and neural cells might determine the passage into the circulation of substances capable

of producing a positive reaction, and sets out to confirm, or refute, the observations of Wolfsohn, Mayer, and Leichert.

His cases, 62 in number, included 39 of chloroform, 12 of ether, and 11 of spinal anaesthesia by stovaine or novocaine, and comprised all kinds of operations. The tests were made simultaneously in more than one laboratory, with blood drawn before and at various times after operation. With the exception of cases in which the reaction was positive before operation there was no single instance of a positive result following the narcosis. The evidence, so far as it goes, is entirely against any influence of anaesthesia on the reaction. E. R. C.

Baggio, G. Il timo studiato negli effetti complessivi della stimizzazione sperimentale. [**The thymus studied in respect of the total effect of experimental removal.**] *Policlin.*, 1922, **30**, Sez. Chir., 197.

In this paper the author returns to the experimental study of the thymus, again using rabbits, although he recognizes that in some respects they are not entirely suitable. In his former work he determined the effect of removal of the thymus in producing a leucopenia, and came to the conclusion, incidentally, that, in respect to blood-changes, the thymus shared with the thyroid in the production of Basedow's symptom-complex. In the present series he is concerned rather with the total result upon the organism as a whole, using as his criteria, duration of life, body-weight, and the weight, after fixation, of the more important endocrine organs. He checks his results with ample controls, but is obliged to make his deductions on percentages, because in every instance there are some contradictory indications. Thus, in the matter of body-weight, some thymus-less animals die lighter than the corresponding controls, but a few heavier. The tendency, however, is very decidedly in favour of lightness—that is, of smaller bodily development, especially when the thymus is removed very soon after birth. Duration of life would seem to be slightly less in the thymus-deprived animal, but when examined after a natural death, no abnormal or imperfect development of the bony skeleton is to be detected in the rabbit, though it seems to be the case with certain other animals. The thyroid, the pituitary, the pancreas, ovaries, and testicles all show, generally, diminution in weight, and the author has previously shown elsewhere that the spleen certainly does not hypertrophy after ablation of the thymus. On the other hand, the suprarenals pretty constantly are found to be decidedly hypertrophied, comparably, in the author's experience, with the hypertrophy of the pituitary observed after removal of the thyroid.

Upon the rather uncertain basis of weight comparisons by percentages, the author offers the suggestion that the thymus belongs to the autonomous 'neuro-vegetative' or vagal system rather than to the sympathetic; that its removal, by diminishing vagal stimulus, leads to over-action of the sympathetic, represented by hypertrophy of the adrenal, hypoplasia of the spleen, and lymphopenia. E. R. C.

Mann, F. C., and **Kawamura, K.** **Duodenectomy.** *Ann. Surg.*, 1922, **75**, 208–20.

While experimental removal of the duodenum had been carried out previously by several investigators, their motive had always been the study of pancreatic function, and any knowledge of the results of duodenectomy

obtained had been of doubtful significance on account of the short life of animals in which any serious interference with the pancreas had been effected.

The authors devised a one-stage operation for removal of the duodenum, with implantation of the bile and pancreatic ducts into the jejunum after end-to-end gastro-jejunostomy. This operation was successfully performed on animals of five species, dog, cat, hog, goat, and monkey. The best results were obtained on the dog, cat, and hog, and conclusions were based on data obtained from experiments on these three species. Provided that the technique of this difficult operation was satisfactory, the animals lived without demonstrable effect on their general health for periods varying from 168 days in the cat, 302 days in the hog, up to 2½ years in the dog. Opaque meals were watched by X-ray in several dogs and no departure from the normal was noted, apart from slight differences in the rate of passage from stomach to intestine in consequence of removal of the pylorus and occasional stenosis of the gastro-jejunal stoma.

In two dogs jejunal ulceration was noted. In one of these the ulcer perforated, causing fatal peritonitis, 515 days after duodenectomy. In the other, a large ulcer with an indurated base was found at necropsy, 383 days after duodenectomy. E. K. M.

Harer, W. B., Hargis, E. H., and **Van Meter, V. C. Studies of the function of the gall-bladder.** *Surg. Gynec. & Obst.*, 1922, **34,** 307.

The authors lay stress upon the fact that but little is known of the function of the gall-bladder. There is much diversity of opinion, varying from that of Hutchison, that the bladder is a vestigial organ, to that of Kemp, that the mucosa changes the bile in such a way as to make it of considerable importance to the organism. Quotations are given from various papers showing the diversity of opinion to-day. In discussing the theory that the organ is vestigial they mention that it has been frequently pointed out that several animals have no gall-bladder, although in them the bile-ducts are considerably larger, thus compensating for the absence of this organ. The gall-bladder has also been frequently removed from the human body with apparently no detrimental effects. On the other hand, they ask the question, 'If it is a vestigial organ, of what is it a vestige and what was its former function?' In the human being only about thirty cases are on record of the complete absence of the gall-bladder. It is as well formed in man as in the lowest vertebrate, and this would not be expected if it were vestigial. They also express doubt as to the belief that the gall-bladder is simply a reservoir for storing surplus bile. The daily secretion of bile probably equals that of the urine, and is from 900 to 1,200 c.cm.; whereas, the normal capacity of the gall-bladder is only about 50 c.cm., and thus it is inadequate to store all the bile secreted between meals. Moreover, the bladder is supplied with a very feeble muscle-layer, which is unable to empty the viscus quickly. Sweet believes that the gall-bladder is emptied by the pressure of the liver and distended stomach. Rhythmic contractions of the gall-bladder have frequently been described, and the wall is said to be relaxed by stimulation of the sympathetic and increased by stimulation of the vagus. Freese showed, however, that the maximum force of contraction exerted by the gall-bladder does not exceed materially the maximum secretion pressure of the bile. Oddi also showed that the sphincter could withstand the

pressure of 700 mm. of water, whereas the gall-bladder contraction is only 313 mm. The authors deduce from this that the contraction of the gall-bladder can have no power in emptying its contents, and thus the theory that the gall-bladder acts as a simple reservoir seems inadequate and untenable.

It is unlikely that the gall-bladder simply acts as a regulator for the flow of bile, for the sphincter of the duct is similarly present whether the gall-bladder be present or absent, but it does, according to Mann, differ in strength. This observer found that the sphincters in animals with a gall-bladder withstand a pressure of 100 mm., whereas those without this organ withstand only 30 mm. of water; but the secretion pressure of the bile was the same in both. They conclude that the flow of bile into the intestine is regulated by the muscle of Oddi rather than by the presence or absence of a gall-bladder.

The theory that the gall-bladder acts as a regulator in preventing the flow of bile up the pancreatic duct is also insufficient, for the pressure of bile in the gall-bladder, common duct, and hepatic duct must be approximately equal, so that in the periods between digestion the pressure in the bile-duct would be about that of the pancreatic duct whether a gall-bladder were present or absent. Moreover, in only about 35 per cent. of all cases is the arrangement of the pancreatic and bile-ducts such as to make regurgitation into the pancreas possible.

The next theory is that the gall-bladder adds something to the bile which is of importance to the general body economy. The bile from the cystic duct is found to be about six times as rich in solids as the hepatic bile, this being chiefly due to the presence of more mucin, sodium taurocholate, sodium glycocholate, and cholesterin, but apparently the gall-bladder adds no new constituent.

The theory that the gall-bladder secretes a hormone which stimulates the flow of bile and pancreatic juice appears to be unsupported. That the gall-bladder is a concentrating organ there can no longer be any doubt, since the work of Rous and McMaster. Judd and Mann found that after removal of the gall-bladder all the ducts outside the liver dilate, the chief factor producing this dilatation being the sphincter of Oddi. Quotations are made showing that after cholecystectomy a large percentage, 69–84, show a deficiency of hydrochloric acid secretion. (It has been the experience of most surgeons, however, that cases of gall-stones show marked hydrochloric acid deficiency before the operation is undertaken.)

The authors carried out a series of experiments on 15 dogs, draining the gall-bladder into the stomach. The outstanding result was that the gall-bladder decreased in size, and where the common duct had been ligated the ducts above dilated. This did not appear to be due to gastric pressure nor to the entry of gastric contents along the ducts, for no such contents were found. X-ray examination with an opaque meal after such an operation also failed to elicit evidence of any regurgitation of gastric contents. They believe that the gall-bladder atrophies and that dilatation of the ducts is a secondary change.

A section then follows describing the gall-bladder lymphatics which the authors regard as of great importance. They believe that the concentration of the bile which takes place in the gall-bladder is due to absorption of the fluid by the lymphatics. In support of this belief they carried out some experiments by using potassium sulpho-cyanide, which was introduced into the gall-bladder and shortly afterwards collected from the left thoracic duct.

They also believe that the lymphatics are the chief connecting links between the gall-bladder, appendix, and pancreas, and that bacteria are carried into the liver and finally enter the bile and so pass to the gall-bladder, where they filter through the lymphatics, from whence they may be carried to the head of the pancreas. A. J. W.

Richter, H. M. Closure of the abdomen without drainage after cholecystectomy and choledochotomy. *Surg. Gynec. & Obst.*, 1922, **34**, 180.

Owing to occasional complications after suture or ligature of the cystic duct followed by closure of the abdomen, it has become usual to adopt post-operative drainage. The present paper is written to show that the abdomen can frequently be closed with safety even when there is a certain amount of infection in the peritoneal cavity. The author's experience of cholecystectomy has shown him that, as the bile-pressure is low, the stump of the cystic duct may be ligatured with fine catgut, and it is unnecessary to embed it or inclose it. In his experience it has never reopened, nor has he found it necessary to cover the resulting raw area of the liver, as the edges tend to fall together. He has found that any biliary leakage from this surface is of trivial importance. He believes that the insertion of a tube leads to frequent reopening of the duct and to fistula formation, and states that it is the drainage material which causes the bile leakage. (This experience is not in accord with that of all surgeons, for the majority have seen cases in which a certain amount of leakage has followed complete closure and has led to a rather troublesome peritonitis, so that anxiety may be felt for a week or more. After that time, however, absorption usually takes place and the patient recovers, but the suspicion is left that there are probably many resulting adhesions.)

In some cases there may be persistent oozing from the liver-surface or unusually active infection or suppuration outside the gall-bladder which may necessitate drainage or packing. Apart from these cases the omission of drainage seems materially to lessen the post-operative discomfort of the patient. Without drainage the average stay in bed has been five days. There has been no hernia in the series.

The advantages are exactly analogous when the common duct can be sutured without drainage, but it is essential that the peritoneum be included in the line of suture and that no stones are left behind or a stricture overlooked. The abdomen, however, should not be closed in the presence of jaundice or acute infection. A. J. W.

Cohen, H. Accessory pancreas with ulcer of pylorus. *Surg. Gynec. & Obst.*, 1922, **34**, 384.

The author points out that the presence of an accessory pancreas is not infrequent. It is more commonly found in adults, but he quotes Hess as having reported one in a child three months old. He states that there are two main theories as to the cause. According to Ruediger, the accessory portion is due to a failure of one of the three embryonic outgrowths to fuse with the main mass. On the other hand, Opie believes that at a very early period of embryonic life a lateral branch of the duct becomes entangled in the mesoblastic layers of the intestinal wall by which it is carried a variable distance from the main duct.

The tumour formed by the accessory pancreas is usually placed between the serous and mucous coats of the intestinal tract. In about one-third of the cases it is situated in the wall of the stomach; most frequently it is in the first eight inches of the jejunum. It may be found in more remote areas such as the ileum, great omentum, hilum of the spleen, and even umbilical fistula. It is unconnected with the main pancreas and has a duct of its own.

Histologically it has a typical pancreatic structure, but often contains no islands of Langerhans. Large bundles of smooth muscle-fibres are present amongst the glandular structures. The mass is usually circumscribed, from 2–6 cm. in diameter and protrudes from the wall of the intestine as a hard nodule, or occasionally projects into the lumen and causes narrowing. It is always covered by the serous intestinal coat. It may undergo similar pathological changes to those affecting the normal gland.

Surgically it may give rise to a diverticulum, to obstruction, to an intussusception, to a pyloric ulcer, or it may become carcinomatous or show acute or chronic inflammatory changes. It has been much doubted whether it is the cause of a pyloric ulcer, and it is also questionable whether the nodule can become carcinomatous.

He gives detailed notes of a case having a characteristic history of a pyloric ulcer. At operation a growth, the size of a hickory nut, was found in the pylorus, causing narrowing of the lumen. A pylorectomy and a posterior gastro-enterostomy were performed. The specimen on examination revealed the presence of a hard nodule composed of the accessory pancreas and opening into the duodenum by its own duct. The mucosa adjacent to the nodule showed superficial ulceration. A. J. W.

Lorey, A. Ueber einen eigenartigen Zwischenfall bei der Anlegung eines Pneumoperitoneums. [**A singular incident in the induction of pneumoperitoneum.**] *München. med. Wchnschr.*, 1922, **3**, 86.

Lorey reports a case in which he induced pneumoperitoneum for the purpose of X-ray diagnosis. When the patient stood up to be screened, she became restless and short of breath with a small rapid pulse. Emphysema then appeared above both clavicles, from which it spread up to the temples and down to the costal margin. The patient recovered completely in two days. He suggests the following explanation.

When the patient stood up the liver dropped and by its weight produced a tear in one of the peritoneal ligaments by which it is attached to the diaphragm. Air then passed through the aortic or oesophageal opening, up the posterior mediastinum, and out into the neck. Since there was no emphysema of the abdominal wall, the air could not have escaped into the tissues at the point of injection. E. K. M.

NEUROLOGY

Gerber, R. Arthritic muscular atrophy with report of a case simulating anterior crural and obturator neuritis. [B.] *Neurol. Bull.*, 1921, **3**, 338.

The author gives the history of clinical observation on arthritic muscular atrophy from the time of Hippocrates to recent times. Brown-Séquard appears to have been the first to ascribe it to reflex irritation, acting through the vasomotor system. Vulpian believed it be due to reflex influence acting on trophic centres in the cord. The first experimental investigations were by Valtat and Dide (1877), while Raymond, in 1890, found that experimentally produced acute arthritis in dogs was followed by muscular atrophy on the side with intact nerve-roots, but was much less, or absent, on the side on which the corresponding dorsal nerve-roots had previously been cut. These results were confirmed by Hoffa in 1892. None of these observers discovered any spinal cord lesion, but Mignot and Mally (1900), in similar experimental studies, reported finding a diminution of anterior horn cells in the lumbar cord after experimental arthritis of the knee-joints. Allen (1911) repeated Raymond's experiments and found that, as soon as the inflammatory reaction in the joint had subsided, there was wasting of the extensor muscles of the joint. The fibres showed simple reduction in size on microscopical examination, but showed absolutely no other pathological change. The peripheral nerves showed no degenerative changes. On the side on which the dorsal nerve-roots had been cut the atrophy was less marked. Nathan (1916), in a discussion on this subject, is quoted as saying that although some nervous symptoms may be reflex in origin in cases of arthritis, yet others are not so. In the case of poly-arthritis he believes that the spinal joints may also be involved, with the production of both spinal cord and spinal root symptoms. It is not clear, however, from the references made to this paper how its writer explains the wasting following a monoarthritis.

Gerber describes a case of arthritis of the left hip where the nervous symptoms resembled those of a lesion of the anterior crural and obturator nerves. There was hypotonus and weakness of ilio-psoas, sartorius, and quadriceps, and wasting of the latter group of muscles. Electrical examination revealed simple diminution of excitability in the affected muscles. The adductor group of muscles were similarly affected, but to a less degree. The tendon-jerks were all normal in the left leg. No very definite sensory change was found objectively, but the patient complained of severe pain in the groin, left hip region, and on the front of the left thigh. This last was the initial symptom and the pain was shooting in character and ran down to below the knee on the inner side of the leg. X-ray examination revealed hypertrophic osteo-arthritis of the left hip. Gerber postulates several possible factors in such a case of arthritic atrophy; disuse from fixation, loss of the normal flow of afferent impulses from joint and muscle, direct action of toxins in the adjacent joint on the muscles, and finally, an essential factor must be a reflex action from the inflamed joints, via the ventral horn cells.

The historical review and the bibliography constitute the chief interest of the paper. F. M. R. W.

Grossman, M. Sequels of acute epidemic encephalitis: A study of ninety-two cases from one to three years after recovery. *J. Am. M. Ass.*, 1922, **78**, 959.

In a previous paper statistics relating to 89 cases of epidemic encephalitis, observed in the second year after apparent recovery, Grossman gave the following tentative prognosis: less than 20 per cent. of cases die during the acute attack. Of those who survive the acute stage, about 10 per cent. may develop a progressive disease of the nervous system. The remainder will make a good functional recovery in from 6 to 24 months after the acute infection, with the probability of progressive approach to the normal after that period.

Unfortunately, the further observations recorded in the present paper do not confirm this relatively optimistic view. 92 patients have been reexamined from one to three years after the acute stage of the disease. Of these, 25 were seen three years after their acute illness, 47 two years, and 20 patients one year. Of the 92, 65 had been under continuous observation from the onset. Of the total number of cases in the series, (1) *10 alone had made a complete recovery* and had no subjective or objective manifestations of nervous disease. (2) 14 others had recovered sufficiently to return to work. Of these, 4 showed facial asymmetry alone, 6 showed this in addition to other cranial nerve defects, while the remaining 4 showed defects of cranial nerve innervation and tremor of face, tongue, or extremities. All but one complained of such psychic symptoms as headache, insomnia, irritability, or depression. (3) In two the symptoms had remained stationary during the previous year. (4) Four patients, although still improving, were far from well, one having bilateral pyramidal tract symptoms and difficulty in swallowing, two showed sluggish pupil reactions to light and tremor in the right arm, one had partial ptosis, a monotonous voice, and bilateral tremor of the hands. (5) The remaining 62 all showed a progressive nervous lesion, which in no less than 42 instances was of the paralysis agitans type clinically.

The paralysis agitans group of 42 cases included 19 females. The ages of the patients ranged from below 10 years (3 cases) to 50 years. 27 were under 30 years. It was not possible to establish any precise interval after the acute illness at which these symptoms developed. But in a few instances a definite interval of freedom from symptoms ranging from four to twelve months was found. Easy fatigability and weakness were the earliest symptoms noted. On the other hand, some patients who during their acute illness showed an intense Parkinsonian symptomatology, were found to be free from this two to three years later.

Cranial nerves. The facial was the nerve most frequently involved, bilaterally in 12, unilaterally in 15. The lesion was always supranuclear in type. The external recti muscles were affected in 9 cases, bilaterally in 3. The internal recti were affected in 3 instances, and there was partial ptosis in 5. One case had almost complete external ophthalmoplegia. The pupils were unequal in 17 cases. In 4 of these the pupils were sluggish to light, and in 2 there was an Argyll-Robertson reaction on both sides. The reverse was found in 2. Irregularity of outline was present in two instances. Horizontal nystagmus was seen twice.

Atrophy and fibrillation of the tongue was seen once, facial twitching twice, and defect of soft palate and uvula once each.

Other symptoms. All the patients showed a mask-like facies, but emotional expression was more facile than in true paralysis agitans. The characteristic attitude of paralysis agitans, retropulsion, and propulsion were present. Tremor of the P.A. type was found in no less than 37 patients, and there was some muscular rigidity observed in 30. In 20 cases the skin reflexes were increased greatly in facility, moderately so in 11, and they were unequal on the opposite sides in 2. In 20 the tendon-jerks were increased, and in 13 they were unequal on the two sides. A Babinski type of plantar response was found in 7 cases, unilaterally in 6 of these. Dribbling of saliva was seen in some cases, while many of the patients had cold cyanosed extremities and a flushed greasy skin on the face. Excessive local sweating was also seen. Many forms of **psychical disturbance** were noted. Psychoneurosis, anxiety states, fear and compulsion neuroses, and hysterical exaggeration of symptoms were common. Most of the patients were drowsy and apathetic during the day. Memory and concentration were defective. In most instances, though progress of the malady was not always clear on examination, nevertheless, all the patients were convinced that they were steadily growing worse.

20 cases remain, not of the paralysis agitans type, in which various cranial nerve defects, alterations of tone and of voluntary movement were present. Tremor was a frequent symptom, and in three instances choreiform movements were present. Psychical disorders were constant and of the type noted above. Three patients showed a myasthenic state.

The author concludes this valuable paper by expressing the view that prognosis as to ultimate recovery from epidemic encephalitis must be guarded even though the patient has survived the acute illness, and by emphasizing that of his series of 92 cases no less than 42 developed the paralysis agitans syndrome. F. M. R. W.

Hörmann. Ein Fall von Polyneuritis nach Arsenvergiftung. [**A case of arsenical polyneuritis.**] *Zentralbl. f. d. ges. Neurol. u. Psychiat.*, 1922, **28**, 242.

A female patient (age not stated) took 4 gm. of a powder containing 88·4 per cent. arsenious acid in mistake for a sleeping medicine. After four hours, vomiting began and recurred each time the patient took a drink. There was no diarrhoea. Paresthesiae were complained of in the hands on the third day, and on the fifth day she began to have delusions, seeing various animals, human figures, and coloured fabrics in her room. She was restless and sleepless. Her mouth ' burned ' and her tongue felt as though covered with splintered glass. The skin of the face and arms was dark coloured and tense, the eyes injected, with oedema of the lids. Headache first developed on the tenth day. Numbness and weakness of the legs began on the twelfth day and spread up to the hands. There was no pain, nor muscular cramp. She was examined at the end of four weeks and was found to have a well-developed polyneuritis with absent tendon-jerks and reaction of degeneration in the thenar muscles. There was astereognosis in the hands, and some cutaneous anaesthesia of the palms. The muscles were tender to pressure. The cerebrospinal fluid contained numerous lymphocytes and an increased globulin content. Mentally, the patient was irritable and showed suicidal tendencies. Arsenic was found in the urine and in the hair. In the discussion which followed the presentation of this

case at the ' Berliner Gesellschaft für Psychiatrie und Nervenkrankheiten ' (12.12.21) two other similar cases were described, in both of which diarrhoea had accompanied the vomiting. In one of these vomiting began on the day following ingestion. F. M. R. W.

Lipschütz, B. Untersuchungen über die Ätiologie der Krankheiten der Herpesgruppen. (Herpes zoster, Herpes genitalis, Herpes febrilis.) [**Studies on the etiology of the herpes group of maladies. (Herpes zoster, Herpes genitalis, Herpes febrilis.)**] *Arch. f. Dermatol. u. Syphilis,* 1921, **136**, 428. (*Zentralbl. f. d. ges. Neurol. u. Psychiat.*, 1922, **28**, 211.)

The different forms of herpes, H. zoster, H. genitalis, and H. febrilis, form a single clinical group and are infectious maladies. In each case the skin lesions contain characteristic intracellular formations, products of reaction of the cells produced under the influence of the virus concerned. In a series of inoculation experiments, using material obtained from the skin lesions in seven cases of herpes zoster, Lipschütz was able to produce a keratitis in rabbits in three instances. In the original and in the experimental lesions he observed ' Zosterkörperchen '. He successfully transmitted herpes genitalis to a second human subject and thence to a third, and also produced a keratitis in a rabbit from the second lesion. In every instance he found in the cell nuclei of the lesion characteristic ' β-bodies '. In herpes febrilis in man, and in a keratitis produced from it by inoculation into the conjunctival sac of a rabbit, he found what he calls ' α-bodies '. He concludes that his experiments confirm the clinically observed differences of these three forms of herpes, and in respect of herpes zoster do not conflict with a widely-held view that this malady is a general infection with a special involvement of the skin. Further researches are in progress.
F. M. R. W.

Simonelli, G. Le insufficienze dell' attività posturale nelle affezioni del cervelletto. [**Deficient postural activity in cerebellar disease.**] *Riv. crit. di clin. med.*, 1921, **22**, 3.

The indeterminate character and lack of precision observed in the movements of patients suffering from cerebellar disease are stated to be due, to some extent at least, to imperfect tonic fixation on the part of certain groups of muscles, whereby the limb or limb-segment is deprived of a firm ' point d'appui ' from which to act. This view has been recently supported by Noica (*Revue Neurologique*, 1921, **28**, 164) in a series of clinical observations, and in two cases recorded by Simonelli. In one of Simonelli's patients both upper and lower limbs were affected ; in the other mainly the lower limb. The phenomena observed by him were as follows :

1. Patient standing : Directed to touch the tip of the nose, the aim was misdirected on to the cheek and the act was accompanied with extensive movements of shoulder, trunk, and pelvis.

2. Patient seated, with one arm hanging free : Aim misdirected and accompanied with movements of the shoulder and oscillation of the trunk.

3. Patient seated, with the trunk supported by one hand resting on the bed : Aim more precise.

4. Patient seated, with trunk and shoulders fixed : Aim more precise and, after the first attempt, approximately correct.

5. Test for dysdiadochokinesis with arm raised: Movement slow and incomplete, and propagated to the arm and shoulder, so that considerable force was required, on the part of the observer, to steady the arm and shoulder, all segments of the patient's limb apparently participating in the movements.

6. The same test, with the elbow fixed to a firm support: Movements more complete and rapid.

7. Walking: In addition to the characteristic features depending on hypermetria and asynergia, movements of the pelvis and irregular oscillations of the trunk were observed.

8. Patient in dorsal decubitus, with leg raised: Directed to make rapid movements of adduction and abduction of the foot, irregular movements of the thigh and pelvis resulted, rendering execution of the directed movements impossible.

9. The same, but with the leg resting on the bed: The alternate movements of the foot were effected slowly and accompanied with alternate rotatory movements of the thigh, which could be prevented only by the use of much force on the part of the observer.

10. Patient seated, with the heel resting on the floor and the thigh fixed by the observer's hands: The alternate movements of the foot were effected in a fairly normal manner. T. W. P. L.

BACTERIOLOGY

Amato, A. Ulteriori ricerche sul sangue degli scarlattinosi. [**Further investigations on the blood of scarlet fever patients.**] *Sperimentale. Arch. di biol.*, 1921, **75**, 383.

The occurrence of certain peculiar bodies within the cytoplasm of polymorphocytes from the blood of scarlet fever patients has been already described by the author (*Sperimentale. Arch. di biol.*, 1913, **67**, 455). He has now had the opportunity of investigating the blood of 24 more cases of scarlet fever in which the presence of the same bodies was again noticed. These bodies are very small, generally round or oval, sometimes elongated, sometimes irregularly triangular or quadrangular, with smoothed corners; they are seldom half-moon shaped. Though generally situated within the polymorphocytes they may occasionally be seen outside them. When stained with Azur II-eosin or with Giemsa's fluid they appear to consist of an external portion coloured pale blue and one or even two or more internal particles purple-red in colour. These bodies of Amato appear to be different from those first described by Döhle (*Centralbl. f. Bakteriol.* (&c.), 1912, Orig. **61**, 63) and then by other authors, because of certain morphological and tinctorial characteristics, and chiefly because in one of Amato's specimens both bodies could be seen. Amato has not as yet formed any definite opinion as to the significance of his bodies; however, he points out that they have a certain resemblance with Lipschütz's strongyloplasms. C. d. F.

Tarozzi, G. (1). Sulle alterazioni anatomiche nella cosidetta encefalite letargica. [**On the anatomical lesions in the so-called lethargic encephalitis.**] *Riforma med.*, 1920, **36**, 320.

Tarozzi, G. (2). Sulla eziologia della encefalite letargica. [**On the aetiology of lethargic encephalitis.**] *Riforma med.*, 1921, **37**, 226.

In his first communication the author pointed out that in the central nervous system of all cases of lethargic encephalitis investigated the characteristic changes of the malady had been found, as well as bronchopneumonic lesions similar to, if not identical with, those commonly seen in cases of influenza. He had therefore come to the conclusion that lethargic encephalitis was either a disease closely related to influenza or perhaps only a form of the latter. In his second note on the subject the author showed how, by means of subdural inoculations into rabbits of the filtered and sterile fluid of cultures of diplo-streptococci isolated from the pulmonary foci referred to above, he had been able to obtain changes of the central nervous system identical with those seen in cases of lethargic encephalitis. Such changes chiefly consisted of meningeal, perivascular, and interstitial infiltrations exclusively formed of 'lymphocytoid cells'. Leucocytes and, apparently, plasma cells were not observed. The rabbits in which these infiltrative changes were found had been killed seven days after the inoculation, and the author is of the opinion that they might have survived much longer and perhaps completely recovered. Some rabbits inoculated subdurally with a very small dose of pure and not filtered cultures from the same diplo-streptococci, died 24 hours afterwards, their central nervous system showing acute infective changes of an oedematous and haemorrhagic character. The subdural inoculation of the same cultures warmed for two hours at 60° C. was not attended by satisfactory results. C. d. F.

Zannelli, P., e Santangelo, G. Contributo alla eziologia della encefalite epidemica. [**On the aetiology of epidemic encephalitis.**] *Ann. d'ig.*, 1921, **31**, 467.

The authors have reached the following conclusions: (1) lethargic encephalitis is caused by a filter-passing virus not as yet morphologically defined; (2) the disease is transmissible to rabbits and guinea-pigs also by means of the cerebrospinal fluid and blood of infected patients; (3) the transmission to animals may be obtained by means of subdural, intraperitoneal, intra-ocular inoculations, as well as through the sub-mucous tissue of the nose, if the mucous membrane was previously artificially altered; (4) the encephalitic virus is transmissible in series; (5) animals of the same species are variously receptive; (6) the results of serial transmissions vary according to the virus used, its virulence being sometimes attenuated, sometimes increased by the passage from animal to animal. C. d. F.

Cavazzuti, A. Sul potere battericida dei sali di tellurio e di selenio. [**On the bactericidal power of the salts of tellurium and selenium.**] *Ann. d'ig.*, 1921, **31**, 551.

The salts of tellurium and selenium have a bactericidal power, strong in the case of tellurium, weak in the case of selenium. The potassium compounds of both tellurium and selenium are more active than the correspondent

sodium compounds. But the bactericidal action of the salts of tellurium and selenium changes also according to the germs used as test; thus they were found to be active on *Staphylococcus pyogenes aureus*, *B. cholerae*, *B. coli communis*, *B. proteus vulgaris*, *B. pyocyaneus*, *B. typhosus*, *B. paratyphosus* A and B, *B. dysenteriae*; not active on the spores of *B. anthracis*.

C. d. F.

Ponder, E. The relation between bile salts and haemolysis in the blood-stream. *Brit. J. Exper. Pathol.*, 1921, **2**, 289.

The bile salts do not cause haemolysis when in the blood-stream: nor does haemoglobinuria follow their injection. This is not due to their forming an absorption product with the albumins of the serum. Since they are colloidal in nature, they are with difficulty excreted by the kidney.

P. F.

Johnson, J. P. Further studies on the production of immunity in rabbits against an organism of high virulence for the species. *Brit. J. Exper. Pathol.*, 1921, **2**, 239.

Experiments are described which demonstrate the possibility of securing the immunity of rabbits against an organism of high virulence by immunization with a live related organism avirulent for the species. In this respect, Tenbroeck's observations are confirmed, and it is further shown that killed vaccines prepared either from the homologous or from a related organism fail to give solid immunity against the live virulent strain. P. F.

Barratt, J. O. W. The theory of agglutinin estimation. *Brit. J. Exper. Pathol.*, 1921, **2**, 214.

1. For a given 'effect' the action between agglutinin and antigen proceeds according to the equation, applicable to a surface action, given by Arrhenius: $yt = m$, y being concentration of agglutinin, t agglutination period, and m a constant.

2. Using a strain of *B. dysenteriae* (Flexner), decay of antigen was found to be represented by the equation $T - a = bt^2$, T being age of suspension of bacilli, t, as before, agglutination period, a and b constants.

3. The relation between y and t given in the first equation is applicable to the estimation of agglutinin in absolute measure if the antigen employed is stable; with antigen subject to decay absolute determinations of agglutinin are still possible for a suitable type of constant b, given by the second equation. P. F.

Johnson, J. P. Comparative immunity tests with saline vaccines and lipovaccines. *Brit. J. Exper. Pathol.*, 1921, **2**, 232.

1. Lipovaccines prepared and employed as indicated stimulate the production of agglutinins to a lesser degree than saline vaccines administered in the same doses. 2. The presence of a high titre of agglutinins does not necessarily indicate the presence of an established immunity even against small doses of a highly virulent organism. P. F.

Yabe, S. The preventive effect of influenza vaccine. *Brit. J. Exper. Pathol.*, 1921, **2**, 223.

When testing the value of protective inoculation against influenza, it is necessary to ensure that the immunization is completed before the epidemic starts. The community to be observed should not have been previously affected, and the test persons and controls should live under absolutely the same conditions. Using a heated influenza vaccine upon a community which responded to those conditions, Yabe found that the morbidity of those inoculated was reduced by a half as compared with the rate of those uninoculated. In other statistics carried out for, but not by, Yabe, in which the inoculation was begun just at the commencement of the epidemic, and was finished by its acme, the morbidity among the inoculated persons, as compared with that among the uninoculated, was reduced to one-sixth by the use of the vaccine. The complications from catarrhal pneumonia were lessened in the case of inoculated patients to one-half and deaths to one-seventh. The length of fever was less among the inoculated persons in proportion to the quantity of vaccine inoculated. The reaction after the inoculation was so slight that cessation from work was unnecessary.

P. F.

Puntoni, V. Un metodo di vaccinazione antirabica con emulsioni fenicate di virus fisso a virulenza graduata. [**Method of antirabic vaccination by means of carbolized emulsions of fixed virus of graduated virulence.**] *Ann. d'ig.*, 1921, **31**, 389.

Fermi's antirabic vaccine (5 gr. of nerve substance from rabbits infected with fixed virus, made into an emulsion with 100 c.cm. of a 1 per cent. solution of carbolic acid, and filtered through a thick wire gauze) has a remarkable vaccinating power even when the virus is completely inactivated by the prolonged action of the carbolic acid (dead carbolized virus). When Fermi's vaccine is prepared by grinding it for 15 minutes in a porcelain mortar and then kept at a temperature of about 21° C., its virulence is attenuated by the carbolic acid in a quite gradual manner so that its subdural virulence is completely destroyed only towards the sixth day. In this way, and by preparing the carbolized virus every day, it is possible to have at one's disposal carbolized emulsions of fixed virus of gradually increasing virulence. These emulsions were tried in the Antirabic Institute of Rome, since January 1920, for vaccinating people bitten by rabid dogs. The results have been very gratifying, and in the opinion of the author more satisfactory than those obtainable by the Pasteur method. For all practical purposes the first injections should be made with 10 days old Fermi's vaccine; subsequently one should use fresher and fresher emulsions until one comes to one day old emulsions, which are very virulent when inoculated subdurally into rabbits but are quite avirulent when injected subcutaneously into partially vaccinated human subjects. The serum of these last has in the end an antirabic power greater than that of the serum of subjects vaccinated by the Pasteur method. C. d. F.

Ecker, E. E. Quantitative relations between amboceptor and the serum of complement-deficient guinea-pigs. *J. Infect. Dis.*, 1921, **29**, 611.

It is well known that certain guinea-pigs are deficient in complement and that the condition is heritable (Moore, 1919). The exact nature of the

deficiency has been investigated by the author, who finds that it is not due to interference with the ambocceptor because increase of the latter leads to haemolysis. The defective sera react in a manner similar to cobra venom inactive serum in that the addition of normal inactive homologous or heterologous sera will markedly enhance haemolysis, confirming the view of Coca (1920) that although the 'mid-piece' and the 'end-piece' of complement are present, the 'third-piece' is lacking and can be supplied by inactive guinea-pig or human serum. Ecker finds that by increase in amboceptor and the addition of normal inactive homologous or heterologous sera the defective serum will act within the usual lytic range of normal guinea-pig serum.

W. B.

Hektoen, L., and **Tunnicliff, Ruth. Opsonic reactivation of antimeningococcus serum.** *J. Infect. Dis.*, 1921, **29**, 553.

In this paper are recorded tables showing the results of opsonic experiments carried out to demonstrate the reactivation of antimeningococcus serum by the addition of fresh normal horse serum. These experiments were carried out to confirm previous results upon which doubt had been cast by Alice C. Evans (*Bull.* No. 124, *Hyg. Lab. Wash.*, p. 43).

G. T. W.

Gay, Jeannette N. An experimental study of saline and lipoid typhoid vaccines in respect to antigenic and immunizing value. [**B.**] *J. Infect. Dis.*, 1921, **29**, 417.

The author records the results of experimental inoculation of rabbits with saline and with lipoid typhoid vaccines. The agglutinin content of the serum was estimated at 4, 8, and 12 weekly periods. The saline vaccine inoculated animals showed good agglutinin response, while the lipoid-vaccine inoculated animals showed no response or only a weak transitory response in the formation of agglutinins. Both series of animals were then inoculated with living cultures of *B. typhosus* and in all cases showed a great increase in agglutination titre. The rise in titre in lipovaccine inoculated animals only differs from the rise in normal animals in appearing a day earlier. The same series of animals was tested by the complement-fixation reaction, but none could be demonstrated. Both series of animals were then tested with regard to their ability to withstand the typhoid carrier condition. Of the control animals 80 per cent. became carriers, while of the saline inoculated animals 30 per cent. and of the lipoid inoculated animals 33⅓ per cent. became carriers. The carriers on autopsy were found to have distended and infected gall-bladders. The author concludes that agglutinin titre is not a measure of protection.

G. T. W.

Lumière, A., et **Couturier, H.** Sur la désensibilisation des animaux anaphylactisés au moyen de plusieurs antigènes. [**The desensitization of animals sensitized with several antigens.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 800.

Lumière and Couturier have carried out the following experiment in order to test the statement that an animal sensitized with several antigens becomes immune to the lot, when once it is protected against any single one of them: A batch of guinea-pigs received subcutaneously 0·5 c.cm. of the following solution on a certain day: dried egg albumin 1 gm., horse serum

2 c.cm., isotonic salt solution 100 c.cm. Ten days later the animals were found to be thoroughly sensitized to both antigens as an intracardiac injection of 5 c.cm. of horse serum or of 3 per cent. egg albumin proved fatal in a few minutes. On the same day (10th) six of the batch of sensitized animals received subcutaneously 1 c.cm. and, two hours later, 2 c.cm. of 3 per cent. egg albumin. These animals were found to be quite desensitized because 5 hours later an intracardiac injection of 0·5 c.cm. of 3 per cent. egg albumin or of horse serum did not prove fatal, only some mild transient effects being noticed. But 20 hours later an intracardiac injection of 0·5 c.cm. of horse serum proved fatal. These experiments were repeated after substituting horse serum for egg albumin, and vice versa, and gave identical results.

The authors conclude that an anaphylactic shock is a specific reaction and that animals sensitized with several antigens and subsequently protected against only one of them will be found to be immune to the other antigens for a very short space of time, viz. under 20 hours. J. R. P.

Manwaring, W. H. Intestinal and hepatic reactions in anaphylaxis. *J. Am. M. Ass.*, 1921, **77**, 849–52.

Manwaring's most important conclusions are that the anaphylactic reaction in guinea-pigs and dogs is characterized by the explosive formation or liberation from the hepatic parenchyma of substances which relax plain muscle. These substances naturally cause general or local (hepatic) vaso-dilatation. In animals in which the phenomena of anaphylaxis are largely respiratory, these substances are beneficial, acting as antispasmodics. The nature of these substances is not determined. G. W.

Bouché, G., et Hustin, A. Le choc sérique léger chez l'homme. [**The slighter manifestations of serum shock in man.**] *Presse méd.*, 1921, **29**, 801-5.

Bouché and Hustin have investigated the reactions which follow the injection of horse serum in man. The injections have been subcutaneous and the doses small, from one-half to two cubic centimetres. Three definite types of reaction have been observed. These are an immediate local reaction, a delayed local reaction, and a generalized reaction. These occur respectively about the first, seventh, and eighteenth days, and any subject may present one or more of these reactions to a single dose. The immediate reaction takes the form of a local redness, swelling and pain, with, maybe, oedema and paresis. It commences within three hours and lasts one to five days. The tache shows a deeper colour at the centre than at the periphery and may become ecchymotic. The delayed local reaction does not parallel in intensity the immediate reaction in the same subject, either directly or indirectly. It consists of a tache reminiscent of a burn of the first degree. It is paler at the centre and is surrounded by a double band of colour, the inner bright red, the outer paler. Its position and extent are those of the immediate reaction. It lasts one to four days. It appears that this reaction may also take the form of urticarial papules of similar distribution. The delayed reaction does not appear to depend on the amount of the dose, for when 2 c.cm. and 10 c.cm. have been given to the same subject but at different points the delayed reaction has been found the same. Bouché and Hustin have further observed with regard to these two reactions that if a second dose be

given within three days of the first the delayed reaction occurs in both about the seventh day, i.e. the delayed reaction to the second dose is hastened. When a second dose is given later than three days from the first the delayed reaction does not occur until the eleventh day, i.e. the reaction from the first dose is still further delayed.

Bouché and Hustin explain these facts as follows: the immediate reaction is produced by the primary toxicity of the serum and the vasomotor reaction is most intense where the toxin is most concentrated, namely, at the centre of the reacting area. The delayed reaction is produced by the interaction of toxin and antitoxin, the latter requiring seven days for its elaboration. It is consequently, they say, a spreading reaction. A ring of reaction appears spreading towards the periphery when the central reaction is complete and vasomotor changes have died down. The antigen-antibody reaction is characterized by two phases, the first of vasoconstriction, the second of vasodilatation. Both of these are due to definite stimulation of the appropriate nerves and not to paralysis of either of them.

The authors next take up the question of the 'injection dechainante' which they induce by a second injection at the same spot as the first. They do not find the phenomena described by Arthus and usually known by his name. The usual symptoms were an immediate swelling which was red, oedematous, and painful. This reached its maximum development in twelve hours and commenced to decline in twenty-four. It is more frequently accompanied by ecchymosis than is the primary reaction. Certain subjects present on the second or third day a bluish discoloration which is not an ecchymosis nor due only to vasodilatation. The authors consider that this is probably due to transient agglutination of red cells in the smaller vessels forming, in effect, temporary thrombi. If secondary injections are made at regular intervals of not more than 30 days, sensitization is maintained. If an interval of 3 months is allowed to elapse, almost no reaction is obtained, but if several months elapse the characteristic reaction for that individual appears. It is noteworthy that individuals tend to have their own type of reaction. Bouché and Hustin give further experimental details, but many of their findings are not yet explicable. Their paper is excellent evidence of the advance in theory which may be expected from this line of research.

G. W.

Torraca, L. L'influenza della narcosi eterea sulla fagocitosi. [**Influence of ether anaesthesia on phagocytosis.**] *Haematologica*, 1920, **1**, 454.

Azzi, A. Azione dei raggi ultravioletti sulla fagocitosi batterica. [**Action of ultra-violet rays on bacteric phagocytosis.**] *Haematologica*, 1920, **1**, 435.

Azzi's investigations continue and conclude those made on the same subject and under his direction by Ciancio (*Riforma med.*, 1919, **35**, 596), Irala (*Medical Science*, 1921, **4**, 460), and Sireci (*Sperimentale, Arch. di biol.*, 1919, **73**, 253). The following results were reached: Staphylococci exposed for a brief time to the action of ultra-violet rays are more easily and more rapidly destroyed by human polymorphocytes than the same germs when untreated. The action of the same rays on both blood and bacteria may favour the phagocytosis still further. However, this action is subordinated to the length of time of the exposure, intensity of the rays, and thickness of the irradiated material. By altering one or the other of these factors, phagocytosis may become less active or be entirely prevented.

Torraca's clinical observations and experiments *in vitro* showed that anaesthesia with ether has an immediate influence on phagocytosis, small doses of the anaesthetic increasing it, and large ones diminishing or preventing it. These phenomena are probably due to a direct action of the ether on phagocytes. C. d. F.

Paolucci, R. Ricerche sulla formazione di sostanze antibatteriche nel sangue *in vitro*. [**On the formation of antibacterial substances in the blood *in vitro*.**] *Haematologica*, 1920, **1**, 523.

Various sets of experiments have led the author to confirm Wright's observation that, by means of bacterial vaccines, antimicrobic properties are made to appear in the blood subtracted from the influence of tissues. These properties, though probably bactericidal, are non-specific, thermolabile, and of a moderate power. For their demonstration appropriate doses of vaccine and bacteria, and repeated microscopic and cultural observations are necessary. C. d. F.

Lattes, L. Sui fattori dell' isoagglutinazione nel sangue umano. [**Factors of isoagglutination of human blood.**] *Haematologica*, 1921, **2**, 401.

As far as the human blood is concerned, agglutination of red blood corpuscles is not merely due to the fixation of the agglutinin, because homogeneous emulsions of corpuscles charged with agglutinin may be obtained; nor is it sufficient, as in the case of certain bacteria, to put the globules in contact with certain electrolytes, practically represented by physiological salt solution. But agglutination is immediately obtained by the addition of any serum even if inactivated at 56° C. In the iso-agglutinating action of human sera two factors or elements can be distinguished: one specific, due to the fixation of the agglutinin on the red blood corpuscles, and one non-specific and thermostabile, existing in the serum independently of the presence of the agglutinin. C. d. F.

Buchanan, J. A., and **Higley, E. T.** **The relationship of blood-groups to disease.** *Brit. J. Exper. Pathol.*, 1921, **2**, 247.

There is no relationship between blood-groups and malignancy as suggested by Alexander (vide *Medical Science*, 1921, **4**, 461). There is no relationship between blood-groups and any disease in which sufficient data are available to justify a conclusion. The percentages originally presented by Moss are approximate and capable of considerable variation, without special significance. Nationality should be taken into consideration in the presentation of statistical studies of blood-grouping. P. F.

Signorelli, E. Il potere complementare del siero durante la proteino-terapia dei morbi infettivi. [**The complement power of the serum during the protein therapy of infectious diseases.**] *Haematologica*, 1920, **1**, 465.

Lura, A., e **Pestalozza, C.** L'influenza delle soluzioni clorosodiche ipertoniche sulla cosidetta anafilatossina da batteri. [**Influence of hypertonic salt solutions on the so-called bacteric anaphylatoxin.**] *Haematologica*, 1920, **1**, 423.

Both papers of Lurà and Pestalozza and Signorelli are connected with the phenomenon known as Friedberger's anaphylatoxin. The results

obtained by the former two authors are a direct confirmation of those reached by Friedberger and can be summarized as follows: the addition of a certain quantity of hypertonic salt solution to the mixture of guinea-pig serum and bacteria (*B. prodigiosus*) prevents the formation of the anaphylatoxin, but if this is already preformed, the addition of NaCl to the mixture of serum plus bacteria plus isotonic salt solution very seldom alters its toxicity. When the formation of the anaphylatoxin is prevented the serum loses at the same time its complement activity. Hypertonic salt solutions act therefore in the same way as heating at 56° C., prolonged shaking, barium chloride, &c., which likewise prevent the formation of the anaphylatoxin and deprive the fresh serum of its complement function.

Signorelli has found that the complement property of the serum of patients affected by various infectious diseases is the same before and after the intravenous injection of heterogeneous vaccines. This appears not to agree with Friedberger's theory of anaphylactic shock, as the complement activity of the serum ought to have been found diminished at least immediately after the inoculation of the heterogeneous vaccines. However, as the complement activity of the human serum is generally very weak, Signorelli puts forward the suggestion that the expected diminution might have been so transitory and slight in character as to escape our present means of investigation. C. d. F.

Sarti, C. Ricerche sui bacilli pseudo-carbonchiosi. Nota I. [**Investigations on pseudo-anthrax bacilli. Note I.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 113.

Among pseudo-anthrax bacilli micro-organisms occur which morphologically and culturally do not differ from *B. anthracis*. These bacilli are not, as a rule, pathogenic for ordinary laboratory animals, but they sometimes give origin to pathological manifestations not very dissimilar from those due to *B. anthracis*. In addition, pseudo-anthrax bacilli possess a great resistance to physical and chemical agents and frequently show the same immunity reactions (precipitation, deviation of complement) as *B. anthracis*. On the other hand there are strains of this last which have no haemolytic action, and bear no spores as in the case of pseudo-anthrax bacilli. Discrimination between *B. anthracis* and *pseudo-anthracis* may, therefore, be very difficult, and always requires a great deal of attention and research. C. d. F.

Svartz, N. Om värdet av blododling vid tyfus. [**The value of blood culture in typhoid fever.**] *Hygeia*, 1921, **83**, 852.

Svartz's survey of the literature is largely concerned with the typhoid epidemic in Jena in 1915, reported on by Schmitz in the following year. In 114 out of 445 cases, blood cultures were made, and positive results were obtained only in 38 per cent. of the 45 cases examined in the first week, in 28 per cent. of the 32 cases examined in the second week, and in a still smaller proportion of cases examined in the third and fourth weeks. Svartz was much more successful. In the period 1919–20 she made blood cultures in 40 cases of typhoid, 10 to 15 c.cm. of blood aspirated from a vein being mixed with ox bile and kept in a thermostat for 24 hours before cultures were made on agar. The results were the following: positive in

all the 12 cases examined in the first week, in 16 of the 22 in the second week, in 4 of the 5 in the third week, and in one of the 2 in the fourth week. Thus positive results were obtained in 83 per cent. Svartz enjoyed the advantage of examining blood taken from patients living under the same roof, and she admits that her percentage of successes would probably have been reduced had the blood been sent her from far afield. On the other hand, she did not, as a rule, repeat the test in negative cases; had she done so, her positive results would probably have been more numerous. The blood of a patient who was still febrile in the eighth week was found at this stage to contain typhoid bacilli. It was examined again 5 days later, when the patient had been afebrile for 4 days, and it was then sterile. Another instructive case was that of a patient who, after being afebrile for 18 days, relapsed in the ninth week of the disease with a sudden rise of temperature. On the second day of this relapse, the blood culture was negative; 2 days later it was positive. In 2 out of 4 cases of paratyphoid B, *bacilli* were found in the blood in the first and second weeks respectively.

C. L.

Murstad, E. Om behandlingen av tyfusbacilbærere. [**The treatment of typhoid carriers.**] *Med. Rev.*, 1921, **38**, 215–34 and 251–72.

At Gade's Pathological Institute in Bergen, the practice has been adopted of taking cultures from the gall-bladder at every necropsy. This led to the discovery of typhoid bacilli in a man of 58, who had contracted typhoid fever 20 years earlier, and had since suffered from slight intermittent pain in the abdomen. Investigation of his past failed to connect him with the origin of any epidemic. When the typhoid bacilli were found, further examination of his organs was made with the following results. Numerous typhoid and coliform colonies from four different parts of the liver, numerous typhoid colonies in pure culture from the intrahepatic bile-ducts, the wall of the gall-bladder, and the interior of gall-stones found in the gall-bladder. The spleen and lungs yielded both typhoid and coliform bacilli. Probably the typhoid bacilli in the two last-named organs reached them after death.

Murstad tabulates the findings of 22 published necropsies on carriers, in 18 of whom typhoid bacilli were found. In most, the liver as well as the gall-bladder contained typhoid bacilli, but Murstad considers that, as a rule, the only permanent abode of these bacilli is the gall-bladder, and that provided this can be removed, the liver will soon cease to be contaminated. In support of this view, he analyses the results of operations on the gall-bladder on 24 carriers. In 4 out of 8 cases in which cholecystostomy was performed, the carrier ceased to carry, and this result was achieved in 15 out of the 16 cases in which cholecystectomy was performed. In the one case in which this operation failed (recorded by Dubs) the excretion of typhoid bacilli had lasted only a few months, and the failure of cholecystectomy in this case hardly applies to the case of the chronic carrier. Murstad's personal experience of cholecystectomy in 3 cases is recorded, in 2 the operation was successful, but in the third it failed, probably because the focus of infection was somewhere else in the intestinal tract. Murstad holds up this case as a warning to operators tempted to remove the gall-bladder without careful and systematic preliminary bacteriological examinations.

The upshot of Murstad's long and interesting discussion is that if the

carrier could be eliminated, typhoid fever would become a very rare disease. He recommends cholecystectomy in the interest of the carrier himself as well as of the community. He has little good to say of vaccine treatment of carriers, or of their medical treatment when the typhoid bacilli are in the stools. But the carriers who excrete typhoid bacilli only in the urine are not infrequently sterilized by drugs, the most effective of which are the formaldehyde group. C. L.

Aoki, K., u. Kondo, S. Beobachtung über die agglutinatorische Veränderlichkeit von Typhusbazillen in homologen Immunsera. [**Observations on the changes in agglutinability of typhoid bacilli in homologous immune sera.**] *Tohoku J. Exper. M.*, 1921, **2**, 357.

The authors found that typhoid bacilli grown in immune typhoid serum become dysagglutinable although this property depends on the race of bacilli employed. A spontaneous agglutination was observed, but it was not very marked in the case of strains which were not easily made dysagglutinable by growth in typhoid serum. If colonies were isolated from a spontaneous agglutinating strain there were two types, a normal one and one which was coarsely granular. Both had the same agglutinability. The dysagglutinability of a strain was maintained for a long time when it was isolated from a dysagglutinable colony. Rabbits injected with a dysagglutinable strain yielded a serum which agglutinated a dysagglutinable strain much better than an ordinary strain. Strains that have been rendered dysagglutinable by growth on immune serum are not identical with those which have become spontaneously dysagglutinable on ordinary agar. W. B.

Faber, H. Die typhösen Knötchen in Leber, Milz und Knochenmark. [**On typhoid nodules in the liver, spleen, and bone marrow.**] *Beitr. z. path. Anat. u. z. allg. Path.*, 1921, **68**, 458.

Conclusions: The occurrence of typhoid nodules in the liver is a regular and specific manifestation of the disease. They show themselves in those places where the liver cells have undergone necrosis, and are due to a proliferation and invasion of histiocytes. Lymphocytes and polymorphocytes take part in the formation of the nodules in very small, though changing, proportions. The moment and intensity of the leucocytic immigration depends upon the extension of the necrosis. If this affects from the beginning not only the liver cells but also the reticulum endothelia, then the leucocytic invasion is the first reactive phenomenon (primary leucocytic immigration). Otherwise the proliferation of the reticulum cells comes first and the leucocytes penetrate into the necrotic foci as a secondary manifestation of the reactive process (secondary leucocytic immigration). Between these two modes of production of typhoid nodules all kinds of transitional and mixed forms can be found. In general the production of typhoid nodules in the liver appears due to toxins probably originating from the elimination of dead or dying typhoid bacilli. The typhoid nodules occurring in the spleen and bone marrow are very likely due to the same histogenetical and aetiological factors. The occurrence of typhoid nodules in the kidneys and other organs may be assumed from a theoretical point of view, but cannot be affirmed with any degree of certainty. C. d. F.

Willführ u. Wendtlandt. Über Massenerkrankungen durch Ratinkulturen. [**On an epidemic produced by cultures of ratin.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 192.

Although it is generally believed that cultures of the type of the Danysz bacillus which is used for rat destruction can be handled by man with impunity, there are several records which point to the fact that it has caused disease in man. The present authors report an outbreak of 95 cases which occurred in a school in Brandenburg. The symptoms were of a gastro-enteritic character and, whereas, 10 were seriously ill, there were no deaths. The infection was traced to 'ratin' bacilli which had been obtained from a neighbouring chemist, and which had been worked up with bread in the kitchen of the school. Of 69 sera which were tested by agglutination with ratin bacilli, 84 per cent. gave positive reactions, the titre with related strains being much lower. W. B.

Schutze, H. The permanence of the serological paratyphoid B types, with observations on the non-specificity of agglutination with 'rough' variants. *J. Hyg.*, 1921, **20**, 330.

This paper deals with the complicated question of the agglutinogenic reactions of types of *B. paratyphosus* B. On the one hand it is held that these agglutinogenic reactions are variable, while on the other, they are believed to be more or less permanent. The author is a supporter of the latter view provided that the existence of what are called 'sub-strains' is recognized, a 'sub-strain' being one which contains less effective agglutinatory antigen than another of the same type. In the author's experience a constancy of type was observed among a large number of strains belonging to the various absorption types of the paratyphoid B group, although the micro-organisms had been kept under observation over a number of years. Two alterations in the serological activity of certain cultures were alone noted. They were due (1) to the appearance of so-called 'rough' variants, (2) to the degeneration of strains into 'sub-strains' which were antigenically less effective. When 'rough' strains are in question agglutination results are equivocal, for a marked cosmopolitanism in respect of this test has been found to exist among such alien species as *B. enteritidis*, *B. paratyphosus* A, and *B. paratyphosus* B. W. B.

Manteuffel, P., u. Beger, H. Weitere Untersuchungen zur Paratyphusfrage, insonderheit zur praktischen Brauchbarkeit des Absättigungsverfahrens für die Typentrennung. [**Further researches on the paratyphoid problem and especially the practical utility of the absorption method for the differentiation of types.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig. **87**, 161.

On a basis of a large experience the authors suggest that the division of paratyphoid bacilli into A and B species should be given up, and that all paratyphoid bacilli should be collected in a common group in which are differentiated type Brion-Kayser (formerly *B. paratyphosus* A), type Schottmüller (formerly *B. paratyphosus* B), type Flügge-Kaensche (formerly *B. paratyphosus* B), type Salmon-Smith (formerly *B. suipestifer*), and type Gärtner (*B. enteritidis*). The differentiation of these types can be made not only by agglutination but by absorption tests. In the latter it is important to use not only a test serum but also a test culture. W. B.

Bender, W. Ein Fall von Septikämie bei einem Säugling, hervorgerufen durch das Bacterium lactis aerogenes. [**Case of septicaemia in a suckling due to *B. lactis aerogenes*.**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig. **87**, 289.

Short account of the bacteriological examination in a child, about eight weeks old, who presented alimentary and nervous symptoms and who died with the appearances of a generalized sepsis. The autopsy revealed pulmonary changes, a whitish-yellow liver, and some hyperaemia of the wall of the intestine with slight swelling of the follicles. Blood taken two or three hours before death yielded pure cultures of an organism that proved to be *B. lactis aerogenes* which in a dose of 0·1 c.cm. of a broth culture was found to be lethal for a mouse. W. B.

Ishi, O. Studies upon agglutination in the colon-typhoid group of bacilli. The preventive action of formalin in the agglutination test. *J. Bact.*, 1922, **7**, 39.

This paper deals especially with the preventive action of formalin in agglutination tests on bacteria of the colon-typhoid group. The author finds that formalin in a concentration of 0·05 to 2·0 per cent. prevents spontaneous agglutination, almost entirely in some instances or completely in others, with *B. typhosus*, *B. paratyphosus* A, and to a less extent with *B. paratyphosus* B. It has no effect on *B. coli*. Agar cultures emulsified with 0·85 per cent. salt solution or neutral broth are almost equal in susceptibility to agglutination. Glucose broth cultures of *B. paratyphosus* A and B and *B. coli* showed a tendency to spontaneous agglutination; *B. typhosus* showed weaker specific agglutination in glucose broth, but stronger than in peptone water. Agar cultures showed much weaker agglutination than broth and peptone water cultures. W. B.

Gärtner, W. Kann der Paratyphus B abdominalis in klinischer, pathologisch-anatomischer, epidemiologischer und bakteriologischer Hinsicht von der sogenannten Gastro-enteritis paratyphosa B abgetrennt werden? [**Can paratyphoid B fever be distinguished from the so-called gastro-enteritis paratyphosa B clinically, anatomically, epidemiologically and bacteriologically?**] *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1922, Orig. **87**, 486.

This is a long paper dealing with the question of the differential diagnosis of the typhoid-like form and the gastro-enteritic form of paratyphoid B. The author considers that these are distinguishable not only symptomatically, but also anatomically and bacteriologically. A large number of observations are collected in support of the author's contention. W. B.

Wadsworth, A. B., and **Vories, R. The action of leucocytes and brain tissue on diphtheria and tetanus toxins.** *J. Immunol.*, 1921, **6**, 413.

Experiments were made to determine whether there is any loss of toxicity in mixtures of diphtheria toxin and the leucocytes of dogs and guinea-pigs such as Wassermann and Takaki (1898) demonstrated with mixtures of tetanus toxin and brain tissue. The free toxin was measured by the intra-cutaneous test in the guinea-pig. In addition to leucocytes, brain tissue of guinea-pigs was also tested for possible neutralizing effect on diphtheria toxin. Although the authors were able to confirm Wassermann

and Takaki's work on tetanus, they found that neither the leucocytes of the dog or the guinea-pig, nor the brain substance of the guinea-pig, exert any neutralizing action on diphtheria toxin. W. B.

Coca, A., Russell, E. F., and Baughman, W. H. The reaction of the rat to diphtheria toxin, with observations on the technic of the Roemer method of testing diphtheria toxin and antitoxin. *J. Immunol.*, 1921, **6**, 387.

The authors demonstrate anew that the rat is highly resistant to diphtheria toxin, but that this resistance is not due to antitoxin normally present in the blood. The rat was found, however, not to be absolutely immune, for although it withstood without ill effect 1,000 times the minimal lethal dose for the guinea-pig, it succumbed in one to three days when the quantity injected subcutaneously was 4,000 M.L.D. After repeated doses of toxin rats can produce antitoxin although not of high titre. The authors claim that the immunity of the rat to diphtheria is due to the property of its cells preventing the toxin entering them or becoming attached to them. In the course of their investigations they found that constant results can be obtained with Römer's method only if larger guinea-pigs (400 gms.) are used. W. B.

Watanabe, Y., Kawatani, M., u. Watanabe, H. Ueber die Beziehungen der im Jahre 1920 in Japan geherrschten Cholerastamme und den El Tor-Vibrionen. [**On the relations between the cholera strains prevailing in Japan in 1920 and El Tor vibrios.**] *Kitasato Arch. of Exper. Med.*, 1921, **4**, 281.

The authors have 48 strains of *V. cholerae* isolated between 1916 and 1920 from cases of cholera occurring in Japan, Korea, and Formosa. They were compared with 56 laboratory strains which included 3 of the well-known 'El Tor' variety. The haemolysin, acid production, agglutinin formation, and absorption, as also the virulence, were examined. All the strains from Japan, Korea, and Formosa were identical except one which was an El Tor. The cholera strains isolated in 1920 were haemolysin producers, but the authors consider that there are no scientific reasons for a differentiation between true and 'para' strains. W. B.

Tron, G. L'immunizzazione attiva contro la difterite. [**Active immunization against diphtheria.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 125.

The preventive treatment of diphtheria by means of active immunization with mixtures of diphtheric toxin and antitoxin can be considered as successfully achieved, particularly after the investigations of Schick. Since, however, the active immunity thus obtained manifests itself after a minimum of three weeks, the method is important only if applied in periods of no epidemics and on a large scale in order to protect children in the years in which they are most receptive to diphtheria. In times of epidemics, and from a therapeutic point of view, passive immunization with large doses of antitoxic serum remains the only method available. C. d. F.

Copeman, S. M., O'Brien, R. A., Eagleton, A. J., and **Glenny, A. T. Experiences with the Schick test and active immunization against diphtheria.**] *Brit. J. Exper. Pathol.*, 1922, **3**, 42.

Three hundred and twenty-nine children between 3 and 16 years of age, in a residential school in which diphtheria had occurred, were examined bacteriologically for the presence of diphtheria bacilli in throat and nose. All giving a positive response to the Schick test were immunized. Eighteen 'morphological diphtheria' carriers were found; 12 cultures were isolated, of which five were virulent. It is suggested that 'avirulent carriers' are unimportant epidemiologically, and that the 'virulent carrier' is dangerous only when virulent bacilli are present in the throat *in large numbers.* Thirty-one per cent. of the children gave a positive Schick reaction; 95 per cent. of the readings made on the first day proved to be correct. Two hundred and three children giving a negative Schick reaction were re-tested 11 weeks later; 2 only gave a positive response; the first negative reaction may have been due to passive immunity resulting from horse diphtheria antitoxin which had been previously administered. Ninety-nine children were immunized with three doses of 1 c.cm. each of toxin-antitoxin mixture; 11 weeks later two only gave clear positive reactions. P. F.

Meyer, Selma. Ein experimenteller Beitrag zur Frage der Pathogenität klinisch virulenter und klinisch avirulenter Diphtheriebacillen. [**An experimental contribution to the pathogenic action of clinically virulent and clinically avirulent diphtheria bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 172.

The author has studied the virulence of diphtheria bacilli in 10 cases of severe and 10 cases of mild diphtheria occurring in children. Guinea-pigs were employed, the test dose of living broth cultures being 0·5 per cent. of the body-weight of the animal inoculated. In 9 out of the 10 clinically severe cases, the bacilli isolated were typically pathogenic for guinea-pigs. There was not the same agreement among the cultures isolated from cases which were clinically mild. Five of the 10 cultures isolated corresponded in being relatively innocuous. In the other 5 the pathogenic effect on the animals was greater than might have been expected considering the mildness of the cases clinically. Bacilli were also tested from temporary and permanent carriers, 9 in number, and with one exception, all were highly pathogenic. Even after a carrier state lasting 3 to 5 months, the virulence of the bacilli was not extinguished although apparently lessened.

W. B.

Rabinowitsch-Kempner, L. Die Bedeutung der Haustiere für die Verbreitung der Tuberkulose. [**The rôle of domestic animals in the dissemination of tuberculosis.**] *Ztschr. f. Tuberk.*, 1921, **34**, 570.

In co-operation with Jost, Lydia Rabinowitsch-Kempner has investigated the frequency of tuberculosis in domestic animals in Berlin, and the types of the tubercle bacilli concerned.

Jost's purely macroscopic examination of 4,683 dogs and 933 cats in 1913 and 1914 showed that the incidence of tuberculosis in the former was 1·6 per cent., and in the latter 11 per cent. Between September 1920 and April 1921, 31 dogs and 6 cats were examined bacteriologically by the authoress, who found tubercle bacilli in 19 of the former and 5 of the latter.

Of the 19 strains cultivated, 16 belonged to the human type, 1 to the bovine type, and 2 were atypical. Of the 5 strains cultivated from cats, 3 belonged to the human, and 2 to the bovine type. She concludes that there has been a considerable increase since 1914 in the frequency of tuberculosis in dogs and cats, the increase being from 1·6 to 2·4 per cent. in the case of dogs, and from 11 to 14·7 per cent. in the case of cats. C. L.

Hirschowitz, B. Über Tuberkulose und ihre Beziehung zu Karzinom, Ulcus ventriculi, Kyphoskoliose und anderweitigen pathologischen Prozessen. [**The relation of tuberculosis to carcinoma, ulcer of the stomach, kypho-scoliosis, and other pathological conditions.**] *Ztschr. f. Tuberk.*, 1922, **35**, 327.

A study of 4,538 necropsies made between 1916 and 1920 inclusive at the German Pathological-Anatomical Institute in Prague has convinced Hirschowitz that the combination of tuberculosis with carcinoma and non-tuberculous kypho-scoliosis is comparatively rare, and that the combination of tuberculosis with gastric ulcer is comparatively common. Only in 4 of the 944 persons dying of tuberculosis was carcinoma found incidentally and in no case were the two conditions found in the same organ. There were, of course, several fatal cases of carcinoma in which tuberculous lesions were found, but these were almost invariably small and healed. Of 2,092 adults in whom tuberculosis was found, only 8·4 per cent. also showed carcinoma, whereas, this was the case in as great a proportion as 10·1 per cent. of the 1,590 persons in whom tuberculosis was not found. The observation is also made that the tuberculosis and carcinoma mortalities in different countries are often inversely proportional to each other, and that Hungary, with the highest tuberculosis mortality (364 per 100,000) of all the States of Middle and Western Europe, had in 1898 the lowest carcinoma mortality (29 per 100,000). Among 2,092 persons over the age of 21 in whom tuberculosis was found, there were 101 (4·9 per cent.) in whom gastric ulcer was also found. The suggestion is made that tuberculosis and gastric ulcer are the expression of a third factor, an asthenic constitution. Of 53 cases of non-tuberculous kypho-scoliosis, only 5 terminated fatally from tuberculosis, and in none of these cases was the degree of spinal curvature very marked. In 29 of these 53 cases, tuberculosis was found at the necropsy, but in as many as 20 the tuberculosis was of old standing and arrested. It would thus seem that the subjects of non-tuberculous spinal curvature are comparatively immune to fatal tuberculosis, and that this immunity is directly proportional to the degree of the deformity of the spine. C. L.

Uhlenhuth, P. Neue Verfahren zur Desinfektion von tuberkulösem Auswurf. [**New procedures for the disinfection of tuberculous sputum.**] *Ztschr. f. Tuberk.*, 1921, **34**, 589.

Uhlenhuth believes that the investigations which he has been conducting over a period of 15 years, and which have entailed the use of more than 1,000 guinea-pigs, have ended in the complete solution of the problem of the sterilization of tuberculous sputum. Every test was repeated 6 to 10 times to eliminate such mistakes as those which have given lysoform, perchloride of mercury, and other disinfectants, an unwarrantable prestige. These were found to be very unreliable, and even antiformin, which disintegrates nummular sputum and destroys most other germs, leaves tubercle bacilli

intact unless the antiformin solution is heated to 55°–60° C. While Uhlenhuth and Joetten were working in 1919 on certain kresol substitutes for soap (which contained no soap, but a small quantity of NaOH) such as K-lysol and Beta-lysol of the firm of Schülke and Mayr, they found to their surprise that they destroyed tubercle bacilli in the sputum. It would seem, as Hailer has also observed, that by the replacement of soap by an alkali in certain kresol solutions, these have been given a remarkable solvent and germicidal property; tubercle bacilli were destroyed within 2 to 4 hours when 100 c.cm. of a 5 per cent. dilution of a solution of alkaline lysol (containing about 4 per cent. alkali and 65 per cent. kresol) were added to 50 c.cm. of sputum. Heated to 80° C., this dilution destroyed tubercle bacilli in half an hour. Particulars are given of various modifications of this compound disinfectant, the action of all of which depends on the presence of an alkali in the disinfectant. C. L.

Heymann, B., u. Koike, M. Über die Beschaffenheit der aus Schildkrötenbazillen hergestellten Tuberkulosemittel. [**The characteristics of tuberculosis remedies prepared from tortoise bacilli.**] *Ztschr. f. Tuberk.*, 1921, **35**, 161.

Friedmann's tortoise bacillus remedy has now got two competitors, for both of which it is claimed that they also are derived from the turtle. One is Piorkowski's, the other Baum's 'vaccine'. Heymann and Koike have examined 52 of Friedmann's ampoules, one of which proved to be contaminated with cocci. Thirty-nine ampoules were tested within the period when they should still be potent; the number of dead and living germs varied greatly. The ratio of living to the total number of germs was also very variable. Of 24 of Baum's ampoules, 4 were contaminated by cocci and other germs, and the content of living germs varied even within wider limits than that of Friedmann's ampoules. The report on Piorkowski's vaccine was still more damning; no time limit for their potency was marked on these ampoules, and of 11 examined immediately after their purchase, only 3 contained living tortoise bacilli, and then only in small numbers. One ampoule certainly contained living germs, but they were only cocci and spore-forming rods. C. L.

Koike, M. Die Lebensdauer der Schildkröten- und Trompetenbacillen im Meerschweinchen und ihr kulturelles und biologisches Verhalten bei Tierpassagen. [**The viability of tortoise and trumpet bacilli in the guinea-pig and their cultural and biological behaviour after animal passage.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 444–92.

In a paper full of details the author has studied the viability of the tortoise and the so-called 'trumpet' acid-fast bacilli in the body of guinea-pigs, the morphology and cultural changes after a sojourn in the body, and the changes in virulence which may ensue. After subcutaneous and intramuscular inoculation in small doses (5–10 mgm.) the bacilli were found alive up to 3 to 5 weeks. A great viability up to 87 days was found after subcutaneous doses of 100 mgm. of culture. Cultures rubbed into the skin lived only 3 or 4 days. Morphologically, no change was found after a sojourn in the body. The growth of the bacilli was much feebler at 37° C. than at 28° C. Persistent attempts to raise the virulence of tortoise or

trumpet bacilli by passage proved without avail, a result contrary to that obtained by Kaufmann, Schröder, and Kolle and Schlossberger.

W. B.

Seitz, A. Zur Differenzierung säurefester Bakterien nach Untersuchungen am Auge. [**The differentiation of acid-fast bacilli by inoculation in the eye.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **33**, 431.

The author has made a comparative study of the effects of inoculating diverse acid-fast bacilli into the anterior chamber of the eyes of rabbits and guinea-pigs. Tubercle bacilli of human and bovine type, the turtle tubercle bacilli of Friedmann, the 'Chelonin' strain of Piorkowski, and saprophytic acid-fast bacilli from milk and from timothy grass were employed. A sharp differentiation of the types by inoculation in the anterior chamber was not possible. Even human apathogenic strains can induce changes in the iris which clinically and anatomically cannot be distinguished from tuberculosis. Inoculation from eye to eye produces no definite increase in virulence. Tubercle bacilli of bovine type do not differ from the others except that from the eye a generalization of the tuberculous process takes place.

W. B.

Holst, P. M. Studies on the effects of tuberculin. *J. Hyg.*, 1921, **20**, 342.

This is a study of the effects and fate of tuberculin when injected into normal animals such as rabbits and guinea-pigs. The test of the existence of tuberculin was made by injection into the skin of tuberculous animals or man. After injection tuberculin rapidly disappears from the vascular system and does not appear in the urine until some hours have elapsed. In the meantime it is fixed in the body, probably in the bones and liver. Living cells *in vitro* can also fix tuberculin. From an extensive series of experiments the author considers that in the complement-fixing tests there are differences between different complements. Tuberculin is highly toxic to leucocytes and more so to cells from tuberculous than from non-tuberculous subjects. A certain protective power in regard to the toxic action of tuberculin is found in serum, and it is more marked in the case of normal than in that from tuberculous subjects. By means of vital staining (Manson's stain) a difference can readily be made out between the effects of tuberculin upon the leucocytes from normal and tuberculous animals. W. B.

Sutherland, P. L. A tuberculosis-like disease in a salt-water fish (halibut) associated with the presence of an acid-fast tubercle-like bacillus. *J. Path. & Bacteriol.*, 1922, **25**, 31.

This is a short account of the occurrence of a tubercle-like disease in halibut which had been condemned as unfit for food. The lesions were found in the liver, spleen, roe, subcutaneous tissues, and muscle, and were granulomatous in character. No giant cells were found. Numerous acid-fast bacilli were present in the lesions, and although these were found to multiply especially at 20° C. a pure culture was not obtained. Two guinea-pigs were inoculated with an emulsion of liver containing many bacilli, but when killed after a month presented no lesions. Three frogs were also inoculated with a negative result. W. B.

Jaffé, R. Ueber die durch säurefeste Bakterien im Säugetierorganismus erzeugten histologischen Veränderungen. [**On the histological changes, in the body of mammals, caused by acid-fast bacteria.**] *Arb. a. d. Staatsinst. f. exper. Therap. u. d. Georg Speyer-Hause zu Frankfurt a. M.*, 1921, Heft **14**, 5.

In a series of 137 animals, mostly guinea-pigs, but occasionally mice and rabbits, the author has investigated the histological changes following the injection of a number of acid-fast bacilli which included human, bovine, avian tubercle bacilli, the tortoise bacilli of Piorkowsky and of Friedmann, the butter bacilli of Rabinowitsch and of Korn, and the timothy grass bacillus of Möller. An elaborate account of the lesions is given, from which the author concludes that all the bacilli employed produce lesions which may be indistinguishable from those produced by mammalian tubercle bacilli. The regressive changes in the lesions may also be similar. The most marked resemblance to genuine tubercle lesions was seen particularly where the saprophytic bacilli had been passed through the mammalian organism.

W. B.

Galassi, C., e Conti, L. Ricerche opsoniche e batteriotropiche nei tubercolosi. [**Opsonic and bacteriotropic investigations in tuberculosis.**] *Boll. d. Soc. med.-chir. di Pavia*, 1921, **34**, 59.

Opsonic activity is very weak in healthy people and tuberculous patients in relatively good conditions; it grows progressively in cases with gradually increasing exudations, in the quickly developing forms and in those characterized by a reabsorption of the effusions, when the opsonic activity reaches its maximum. The bacteriotropic activity is, on the contrary, very weak in healthy subjects and in severe forms of tuberculosis, it becomes more and more noticeable in less severe cases, and in sclerotic forms characterized by relatively good or even very good general conditions.

C. d. F.

Fiori, P. Osservazioni sopra germi anaerobi. [**Observations on anaerobic germs.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 65.

The present paper continues and completes studies to which reference has already been made (*Medical Science*, 1920, **2**, 375). The author has now investigated the modifications of strain 10 of *B. perfringens* isolated by him from war wounds. The fundamental characteristics of the species remained unchanged, but a fresh tendency to the formation of filaments in agar cultures and to the production of spores were noticed. In addition, the strain acquired a very strong pathogenic power for the rabbit, in which haemolytic phenomena were observed similar to those due to a strain of *B. anthracis symptomatici* used for comparison. C. d. F.

Heller, Hilda H. **Notes on the genus Nicolaierillus (*B. tetani*).** *J. Infect. Dis.*, 1922, **30**, 18.

Under the dissonant name *Nicolaierillus* the authoress has made a study of *Bacillus tetani* in its cultural and morphological characteristics. She believes that tetanus strains show remarkable powers of mutation on complex protein media. The behaviour of pure cultures on meat medium is

fairly characteristic, and this medium is probably the best for detecting common contaminating anaerobes in a culture of *B. tetani* believed to be pure. All the strains of *B. tetani* examined were definitely proteolytic, but none were intensely so. We cannot think that the new designation of *Macintoshillus* suggested by the authoress for *Bacillus tetanomorphus*, the name given by the Anaerobic Committee of the M.R.C., will become part of permanent bacteriological nomenclature. W. B.

Heller, Hilda H. The study of colony formation in deep agar. *J. Infect. Dis.*, 1922, **30**, 1.

The authoress claims that under constant conditions members of a pure culture of anaerobic bacteria give rise to deep colonies that are almost constant in type. It is also claimed that different anaerobic bacilli which correspond in all ordinary cultural characteristics may be differentiated into groups of strains on the basis of colony formation in deep agar. The shape of a colony in an agar medium depends primarily on the reproductive power of an organism and its motility. The reproductive power depends on its enzymes and metabolic activities. Any mutation, therefore, involving the metabolic activities of the organism on a given medium may demonstrate its occurrence by causing a change in the colony morphology of the mutating organisms in the strain. The paper is illustrated by many photographs of colonies. W. B.

Heller, Hilda H. Mutations in the genus Nicolaierillus (*B. tetani*). *J. Infect. Dis.*, 1922, **30**, 33.

The authoress has made a detailed study of a large number of strains of *B. tetani*, and considers that they mutate readily in protein media in which they are able to multiply actively. These mutations refer to colony formation, and have no influence on the morphology of the bacilli themselves. No effect on toxin formation was noted in the colony mutations. The paper is illustrated with many photographic reproductions of colonies. W. B.

Orr, P. F. The pathogenicity of *Bacillus botulinus*. [B.] *J. Infect. Dis.*, 1922, **30**, 118.

A series of observations are detailed to show that, contrary to the older view, the optimum temperature for growth and toxin production by *B. botulinus* is 37° C. Further, *B. botulinus* can be recovered from the internal organs of animals fed or injected with toxic cultures or toxin-free spores. Under certain conditions, e.g. by feeding with spores, *B. botulinus* will grow in the body of the guinea-pig and produce toxin. The presence of toxin produced in the body as a result of the growth of toxin-free spores in the body can be shown by the precipitin test as well as by direct toxic effects. In man, poisoning by ingestion of botulinus spores is probably very rare if it occurs at all. W. B.

Henry, H. On *B. welchii* haemotoxin and its neutralization with antitoxin. *J. Path. & Bacteriol.*, 1922, **25**, 1.

This research deals with the haemotoxin present in cultures of *B. welchii* and its neutralization by antihaemotoxin. The toxin was tested *in vitro* on the washed corpuscles of rabbits, the titre being estimated by using a haemoglobin scale. Stored in the cold, the haemotoxin suffered but little depreciation in 6 weeks, whereas at 38° C. its potency was reduced to one-half at the end of 10 days. A large part of the haemotoxic power is lost by heating to 60° C. for 5 minutes, although a certain fraction will survive this temperature and even higher temperatures for some time. Even boiling for 15 minutes does not destroy the toxin completely. It can also be neutralized by antitoxin, the combination between toxin and antitoxin taking place relatively quickly. Experiments indicated that the union of toxin and antitoxin obeys the law of multiple proportion. W. B.

Heller, Hilda H. Certain genera of the *Clostridiaceae*. Studies in pathogenic anaerobes. V. *J. Bact.*, 1922, **7**, 1.

In this paper the authoress discusses the classification of the bacillary pathogenic anaerobes and suggests for them a new name, *Clostridiaceae*, with two sub-families *Putrificoideae* or proteolytic anaerobes and *Clostridioideae* or non-proteolytic anaerobes. Wholesale changes are suggested in the nomenclature of well-known anaerobic bacilli, the new name being the suffix 'illus' to whole or part of the name of the discoverer of the organism. Thus it is suggested that *B. sporogenes* should be now called *Metchnikovillus*; *B. chauvoei* becomes *Arloingillus*; *B. egens* is altered to *Stoddardillus*, *B. welchii* to *Welchillus*. English workers on anaerobes will be recognized in such designations as *Macintoshillus*, *Douglasillus*, *Flemingillus*, *Robertsonillus*, and *Henrillus*. The etymology of *Reglillus* and *Vallorillus* is not apparent. Difficulties in a nomenclature of this kind intrude themselves when one author has discovered more than one anaerobe. Thus in addition to *B. egens* (now called *Stoddardillus*) Stoddard discovered *B. multifermentans-tenalbus* and the new generic name suggested for this microbe is *Multifermentans-tenalbus*. W. B

BIOCHEMISTRY

Barát, I., u. Hetényi, G. Der Reststickstoff im menschlichen Blut und Gewebe bei Nierenerkrankungen. [**Rest nitrogen in blood and tissues in renal disease.**] *Deutsches Arch. f. klin. Med.*, 1922, **138**, 154.

The rest nitrogen in human blood and tissue was examined in cases of nephritis either during an operation or shortly after death. They found the rest nitrogen contained in the tissues was higher than that in the blood in normal subjects. There is a distinct increase in the amount of rest nitrogen in the tissues in diffuse haematogenous affections of the kidney. In acute nephritic conditions the percentage increase of the blood rest nitrogen is

greater than that of the tissues. The converse is the case in nephroses, amyloid conditions, and toxic nephritis. In chronic conditions the percentage increase is the same in the blood and in the tissues. C. G. L. W.

Straub, H., u. Meier, K. Blutreaktion und Dyspnoë bei Nierenkrankheiten. [**Blood reaction and dyspnoea in renal disease.**] *Deutsches Arch. f. klin. Med.*, 1922, **138**, 208.

The carbon dioxide combining curve of the blood and the carbon dioxide pressure of the alveolar air were determined in 21 cases of nephritis, and from these 21 determinations the actual reaction of the blood was estimated. In spite of renal disturbance the reaction varies only between P_H 7·30 and P_H 7·40. In many cases with a decreased carbon dioxide combining curve (hypocapnia) the carbon dioxide pressure in the lungs is depressed by over-breathing to such an extent that the reaction of the blood remains normal. When this excessive ventilation does not take place the blood becomes acid. The dyspnoea in these cases is due to a primary blood change. The dyspnoea which occurs in the later stages of renal insufficiency is a true uraemic dyspnoea. There are other cases in which excessive breathing is associated with a depression of the carbon dioxide partial pressure in the lungs. Although the carbon dioxide combining curve remains normal or hypercapnic, the blood reaction in these cases tends towards the alkaline side. The over-breathing is central in origin and probably depends upon an asphyxia of the respiratory centre due to local disturbances of circulation. This form of dyspnoea is not uraemic. This is a form that is seen in the early stages of the disease and is known as hypotonic cerebral asthma. C. G. L. W.

Schade, H. Die physikochemischen Gesetzmässigkeiten des Harnsäurekolloids und die übersättigten Harnsäurelösungen. [**The physical chemistry of colloidal uric acid and of supersaturated solution of this acid.**] *Ztschr. f. klin. Med.*, 1922, **93**, 1.

In a previous paper with Boden, Schade has shown that the precipitation of uric acid from a supersaturated solution is an intermediary step in its colloidal condition, and has pointed out the practical consequences of this in the aetiology of gout. They made out that the urates in the blood may be in a colloidal condition, and, as the result of a disturbance in this condition at any one point, conditions for precipitation may be favoured. The present elaborate paper is a further contribution to this subject in which the physicochemical properties of supersaturated uric acid conditions are taken up. Among the interesting features of this investigation are the effects which small amounts of acid or alkali produce on the form of precipitation of uric acid. Near the neutral zone precipitation takes place in extremely minute spherical particles. With small amounts of acid or alkali the deposit becomes crystalline, increasing in this character according to the amount of alkali or acid added. C. G. L. W.

Richards, A. N., and **Plant, O. H.** **Urine formation in the perfused kidney. I. The influence of alteration in renal blood-pressure on the amount and composition of urine. II. The influence of adrenalin on the volume of the perfused kidney. III. The action of minute doses of adrenalin and pituitrin on the kidney.** *Am. J. Physiol.*, 1922, **59**, 144, 184, 191.

A contribution to the discussion whether the formation of urine is essentially a process of filtration or of secretion. The experiments were arranged so that it was possible to alter the pressure within the renal circulation without altering the blood-flow through the organ. Changes in pressure were accompanied by parallel changes in the rate of urine elimination. The evidence is therefore in support of the filtration theory of glomerular function. W. C.

Binswanger, F. Über Einwirkung der Kohlensäure auf den Blutzucker im Organismus. [**The effect of carbon dioxide on the blood-sugar in the body.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 296.

When rabbits or cats were given oxygen-carbon dioxide mixtures, containing from 6 to 30 per cent. of carbon dioxide, to breathe, hyperglycaemia resulted. Attempts were made to find the cause of this. It appeared to be independent of the central nervous system, and also independent of the increased hydrogen-ion concentration of the blood. C. L. E.

Pickering, J. W., and **Hewitt, J. A.** **Studies of the coagulation of the blood. Part I. Some physico-chemical aspects of coagulation.** *Biochem. J.*, 1921, **15**, 710.

In the slow precipitation of gelatin by alcohol, a condition has been found closely analogous to the negative phase of blood-coagulation and to the Dansyz reaction. Filtered tissue extract added gradually to birds' blood produced a temporary negative phase. When added quickly coagulation is produced. The occurrence of thrombosis in normal circulating plasma is a phenomenon similar to the negative phase and is probably a physical process. In shed mammalian blood the formation of a reversible gel induces the formation of a true clot. Many of the recognized facts of blood-coagulation are explicable as physical phenomena. Attention is directed to the respective electrical charges of accelerators and inhibitors of blood-coagulation, also to the similarity of their electric condition to those associated respectively with precipitation and maintenance of solution. It is suggested that coagulation of the blood commences as a physical and reversible process and ends in a chemical reaction in which there are at least two products, namely, fibrin and thrombin. C. G. L. W.

Abderhalden, E. Weitere Forschungen über die Senkungsgeschwindigkeit der roten Blutkörperchen bei gleichen und bei verschiedenen Tierarten und unter versch. Bedingungen. [**Further researches on the velocity of sedimentation of the red corpuscles of the same and of different animals and under various conditions.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 236.

The author attempts to answer the question why the bottom layer of corpuscles in the centrifuged corpuscular mud finds itself there: is it mere chance, or is it because the corpuscles on centrifugation arrange themselves

as they do because of some differences in physical properties? The answer seems to be in favour of the latter alternative, because when re-suspended the bottom layer has a higher sedimentation-rate than the upper layers. The rate of sedimentation is, as other authors have frequently found, greatly influenced by the composition of the blood-plasma, and especially by the presence of foreign plasma, even in minute traces. In the other parts of the paper many questions are asked, but the answers are few.

C. L. E.

Jencks, Z. Studies in the regeneration of blood. *Am. J. Physiol.*, 1922, **59**, 240.

Haemorrhages were induced in rats amounting to one-third of the estimated total blood-volume. The speed of regeneration was measured by the length of time necessary for the return of the number of red cells and the haemoglobin percentage to the values observed before the haemorrhage. The effect of different diets was studied. Diets rich in vitamins accelerated regeneration as compared with diets free from vitamins. W. C.

Morris, J. L., and **Macleod, A. G. I. Colorimetric determination of uric acid. Estimation of 0·03 to 0·5 mg. quantities by a new method. II. Studies on the uric acid of human blood.** *J. Biol. Chem.*, 1922, **50**, 55.

A new method of estimating uric acid is described, involving a Zn precipitation combined with a colorimetric method. From a preliminary investigation of uric acid in human blood, it appears that there is discrepancy between the method described above and the 'Folin and Wu' method of estimation. The 'Folin and Wu' gives in many cases a lower value for the uric acid. The authors think that uric acid exists in two forms in human blood, one of which is not estimated by the 'Folin and Wu' method. Uric acid is found to be present in both the corpuscles and the serum of human blood, though there is more in the serum. This is contrary to the results obtained upon other animals, and indicates a special position of man in this respect. Benedict, for instance, has found that in ox blood all the uric acid (free and combined) is present in the corpuscles. It is suggested tentatively that the second form of uric acid in human blood is different to the second form in ox blood, but it is hoped to clear up these points in future research.

R. A. P.

Atzler, E., u. **Lehmann, G.** Weitere Untersuchungen über den Einfluss der Wasserstoffionenkonzentration auf die Blutgefässe unter besonderer Berücksichtigung des Pufferungsgrades der Durchströmungsflüssigkeit. [**Further investigations on the influence of the hydrogen-ion concentration on the blood-vessels, with especial reference to the buffering of the perfusion fluid.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 463.

The authors have previously shown that, on either side of a given range over which change of hydrogen-ion concentration is ineffective, an increase of either the hydrogen- or hydroxyl-ion concentration (that is to say either increase or decrease of the hydrogen-ion concentration) causes contraction of the blood-vessels, as judged from experiments on the perfused frog's limbs. It is now shown that the boundaries of this neutral zone largely depend on the extent to which the (ingoing) perfusion fluid is buffered. The less the

solution is buffered the wider is the neutral zone. Thus, with strongly buffered solutions such as those containing 1/3 molar phosphate, the zone extends from P_H 5·65 to 6·6; in more weakly buffered solutions (m/39 phosphate) it reaches from P_H 4·2 to 7·45, while in completely unbuffered solutions the limits are between P_H 2·9 and 9·35. The reason is that the more lightly the solution is buffered the easier it is for the tissue to add ampholytes which will adjust the reaction of the fluid in contact with the tissues to that of the normal circulating blood of the animal, which would thus appear to be somewhere about P_H 6 for the frog. C. L. E.

Deusch, G. Über die Serumkonzentration und die Viskosität des Blutes bei der Basedow'schen Krankheit. [**Serum concentration and viscosity in Basedow's disease.**] *Deutsches Arch. f. klin. Med.*, 1922, **138**, 175.

In a former paper the author showed that in consequence of the decrease of nitrogen metabolism in myxoedema there was an increase in the albumin content and the viscosity of the blood-serum which might reach a very high value. He has investigated 11 cases of Basedow's disease and found that in advanced cases the protein content of the blood-serum is decreased, the viscosity is also low. He was able to make out changes towards the normal in cases which were undergoing successful treatment. It is suggested that the method might be used in order to follow out the condition of the case without an examination of the respiratory exchange. C. G. L. W.

Yabe, S. The action of diphtheria toxin on the circulation. *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 1.

Cats were decerebrated under ether and the blood-pressure and respiration studied after an injection of a killed bouillon culture of *B. diphtheriae*. The effects are delayed for many hours. After injection the blood-pressure is lowered, and this appears to be due to failure of the central vasomotor mechanism. No evidence of direct action on the peripheral vasoconstrictor nerves or on the vessels of the heart was obtained. C. G. L. W.

Schleier, J. Der Einfluss gefässerregender Mittel auf die Elastizität der Arterienwand. [**The influence of vascular excitants on the elasticity of the artery walls.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 610.

The experiments were made on the hind-leg preparation of the frog, perfused under increasing and diminishing pressures with saline solutions, both before and after the addition of adrenalin and barium chloride. The hydrodynamic conditions were deduced from measurements of the pressures and rate of flow in the vessels. At higher pressures there was evidence that the contracted arteries were more distensible than the more relaxed ones. It is suggested that this fact may explain the superiority of pulsating over constant pressures for perfusion experiments. C. L. E.

Cunningham, R. S. On the origin of the free cells of serous exudates. [**B.**] *Am. J. Physiol.*, 1922, **59**, 1.

The paper contains a concise and very clear discussion of the various views held on this controversial and difficult subject. The author's experimental observations lead him to the following general conclusion: there

are great groups of cells which have been differentiated from the primitive mesoderm and have developed certain special characteristics in response to the varying needs of the organism. All of these cells retain some of the more primitive reactions of the mesoderm, and some of them retain sufficient of these characteristics to be able, under stimulation, to develop into more highly differentiated cells. These cells, which almost certainly retain the capability of forming new cells of a more highly specialized character, are the reticulum and endothelium of spleen and lymph glands. These give origin to the large mononuclear cells of the blood. On the other hand, the fibroblast, the clasmatocyte, and the serosal lining cell cannot undergo any such differentiation. These are distinct types of highly specialized cell with specific functions.

It is possible that the general vascular endothelium and the lining cells of the subarachnoid may give rise to free cells, but the evidence is not yet conclusive.

The paper, which cannot be abstracted adequately, should be read in the original. W. C.

Frey, W., u. Hageman, E. Die Brauchbarkeit der Adrenalinlymphocytose zur Funktionsprüfung der Milz. Klinisches und experimentelles Beweismaterial. [**Adrenalin lymphocytosis as a test for splenic function.**] *Ztschr. f. klin. Med.*, 1921, **92**, 450.

It has been shown that 20 minutes after an injection of 1 mm. adrenalin into man a lymphocytosis takes place in which the number of these cells may be as high as 2,500. This appears to be due to a mechanical mobilization of lymphocytic elements in the spleen. The authors have attempted to ascertain whether pathological conditions of the spleen can be detected by the absence of this phenomenon. Sixteen cases of splenomegaly were investigated before operation, and the condition of the spleen ascertained from the histological picture. In only one case did the adrenalin test give a doubtful result. A negative reaction to the test indicates a severe pathological condition of the splenic tissue. The degree of lymphocytosis is dependent upon splenic function. A negative test is given when the number of leucocytes is decreased to less than 1,500 20 minutes after injection. C. G. L. W.

Arnoldi, W., u. Leschke, E. Die Wirkung der aus endokrinen Drüsen hergestellten Präparate auf den Gaswechsel. [**The action of endocrine preparations on respiratory metabolism.**] *Ztschr. f. klin. Med.*, 1921, **92**, 364.

Experiments were made on the respiratory exchange and the nitrogen balance in a young under-nourished woman to whom was administered thymin, the extracts of the anterior and the posterior lobes of the pituitary, thyroid preparation, adrenalin, and luteoglandol (an ovarian preparation) during various stages of carbohydrate nutrition. It was found that the effect of these preparations on metabolism depends upon the condition of nutrition of the patient, especially the amount of carbohydrate which is being consumed. With large doses a marked effect of the drugs is obtained and proteins are catabolized along with carbohydrate. When the amount of carbohydrate administered at the same time is large there is a reduction of water and salts excreted and the weight of the patient increased.
C. G. L. W.

Marine, D., and **Baumann, E. J.** **Influence of glands with internal secretions upon the respiratory exchange. III. Effect of suprarenal insufficiency (by removal) in thyroidectomized rabbits.** *Am. J. Physiol.*, 1922, **59**, 353.

Removal of the adrenals leads, in rabbits, frequently to increased heat-production. This is attributed to the absence of the cortex. If previous to adrenalectomy the thyroids have been removed this rise in heat production is prevented. It is therefore dependent on the presence of the thyroid gland and is due to an increased functional activity of this gland. The authors make the speculative suggestion that the cortex exercises a restraining or inhibitory control over the thyroid gland, while the medulla, by secreting adrenalin, can stimulate the thyroid. They also suggest, on the basis of this speculation, that exophthalmic goitre may be due to loss of cortical control over the thyroid through weakness or exhaustion of the cortical function. W. C.

Loevænhart, A. S., Malone, J. Y., and **Martin, H. G.** **The action of respiratory stimulants upon the respiration when depressed by increased intracranial pressure, with special reference to sodium cyanide.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 13.

This work was suggested by a case of increased intracranial pressure, due to severe cerebral oedema, in which the respiration became depressed and the problem of selecting a suitable stimulant was presented. The authors find that sodium cyanide is the most reliable stimulant to the respiration when depressed by increased intracranial pressure. The changes in the blood-pressure following therapeutic doses are insignificant. The effects are brief but, by giving cyanide continuously, stimulation of the respiration may be maintained for hours. The drug must be administered intravenously. Strychnine is also a stimulant, but the effect is not so prompt nor so reliable as in the case of sodium cyanide. The duration of stimulation may be 20 to 60 minutes. Atropine is most unreliable. With caffein a brief but definite stimulation of the respiration can be obtained.
C. G. L. W.

Craigie, E. H. **The reflex produced by chemical stimulation of the deeper respiratory passages.** *Am. J. Physiol.*, 1922, **59**, 346.

Experiments on dogs. The respiratory reflex obtained by stimulation of the deeper respiratory passages with ammonia vapour or ether, consists of an increased expiratory effort and an inhibition of respiration. These two effects appear in varying proportions. The vasomotor response consists of a gradual fall in blood-pressure, followed at once by a somewhat slower return to the normal. The disputed question whether the integrity of the vagus nerve is essential for the production of these reflexes is answered by the author in the negative. The reflexes are entirely unaffected by the section of both vagi. The afferent impulses concerned pass probably through the sympathetic into the spinal cord and travel up into the medulla oblongata. W. C.

Black, E. M., Hupper, M., and **Rogers, J. The effect of adrenal feeding upon the iodine content of the thyroid gland.** *Am. J. Physiol.*, 1922, **59**, 222.

Feeding with a protein-free extract of the entire adrenal gland produces a distinct increase in the iodine content of the thyroid gland. The extract contained some adrenalin, but a corresponding amount of pure adrenalin alone produced a distinctly smaller increase in the iodine content.

W. C.

Liljestrand, G., u. **Magnus, R.** Die Wirkung des Kohlensäurebades beim Gesunden nebst Bemerkungen über den Einfluss des Hochgebirges. [**The effects of carbonic acid baths on normal individuals, with observations on high altitudes.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 527.

Experiments were made at Bad St. Moritz, which is situated at an altitude of 1,800 metres. At this altitude the post absorptive basal metabolism, the minute output of blood from the heart, and also the (unreduced) pulmonary ventilation were the same as at ordinary levels. The alveolar CO_2 pressure was slightly lowered, and there was also a lowering of venous CO_2 pressures amounting to between 4·0 and 5·7 mm.

When the subject was immersed in a tepid carbonic acid bath (temperature 33° C.), there was conspicuous dilatation of the skin vessels, accompanied by a subjective sensation of warmth. The basal metabolism was not increased either during or after the bath, with the consequence that the body temperature was lowered by 1° C. or even more. These effects of carbon dioxide are stated to be due to a direct action of the substance on the skin vessels; as a compensation for the dilatation the output of the heart per minute was in some cases increased, though in all cases there was a fall in the pulse-rate owing to the cooling of the body. The respiratory ventilation is increased during immersion in the bath, even when pure air free from carbon dioxide was breathed; the carbon dioxide tension in the blood was correspondingly reduced. C. L. E.

Storm van Leeuwen, W., and **von Szent-György, A. On scopolamine-morphine narcosis.** *J. Pharmacol. & Exper. Therap.*, 1922, **18**, 449.

According to Schneiderlin 2 mgm. of scopolamine or 60 mgm. of morphine when given to an adult do not produce narcotic symptoms, whilst half the dose of the first drug combined with half the dose of the second leads to narcosis of more than two hours' duration. This synergistic action of scopolamine and morphine does not exert itself clearly in all cases where it has been tried in man. The question as to whether scopolamine potentiates morphine has not been definitely settled. The authors performed experiments on monkeys and found that this animal is very sensitive to small doses of morphine, while 20 times the dose of scopolamine does not produce any visible effect. Scopolamine does not augment the action of morphine on monkeys so far as concerns the external symptoms produced by this drug. C. G. L. W.

Bonar, M. L., and **Sollmann, T.** **The effect of some new local anaesthetics (para-aminobenzoyl dinormal butyl-amino ethanol and propanol, and diethyl-amino propyl-diphenyl-amino-carbinol).** *J. Pharmacol. & Exper. Therap.*, 1922, **18**, 467.

Amino-benzol-dibutyl-amino-propanol hydrochloride was found to produce complete anaesthesia on surface application to mucous membranes such as the conjunctivae in concentrations about one-half of those of cocaine, one-tenth those of procaine, and about the same of holocaine. It has the important advantage of being non-irritant. It does not affect the blood-vessels materially and can be used with adrenalin. It holds out promise of usefulness for anaesthesia of intact mucous membranes, especially in the eye, a field that has not so far been satisfactorily filled by synthetic anaesthetics. The other compounds were less useful. C. G. L. W.

Mast, S. O., and **Ibara, Y.** **Effect of ethyl alcohol on tadpoles.** *Am. J. Physiol.*, 1922, **59**, 294.

Tadpoles were kept in tap-water containing a small amount of alcohol. The concentrations used varied from $\frac{2}{3}$ per cent. to $\frac{1}{3}$ per cent. The tadpoles were compared as regards rate of growth and mortality with tadpoles kept in tap-water alone. The effect of the presence or absence of food given in the form of certain plants was also studied. The experiments gave the surprising result that the tadpoles kept in the tap-water containing alcohol grew more rapidly and showed a greatly reduced rate of mortality.

W. C.

Abelin, I. Die Frage der Wirkung jodierter Eiweisskörper auf die Metamorphose von Froschlarven. [**The effect of iodized proteins on the metamorphosis of tadpoles.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 624.

Iodized casein was found to accelerate metamorphosis, while iodized gelatin was inactive. The chemical constitution of the substance which accelerates the change is therefore more important than its mere iodine content, and not all protein structures are suitable. Perhaps it is some individual amino-acid of the protein which is active; certainly diiodotyrosine and diiododyramine are both active. C. L. E.

Stewart, G. N., and **Rogoff, J. M.** **The influence of morphine on normal cats and on cats deprived of the greater part of the adrenals, with special reference to body temperature, pulse and respiratory frequency, and blood-sugar content.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 97.

There is no close association between the hyperthermia (as much as 4° C.) produced by morphine in cats and the hyperglycaemia or the degree of muscular activity. The hyperthermia and general symptoms develop in the same way and reach the same intensity in cats from which the greater portion of the adrenal tissue has been removed and the remaining fragment denervated, as in normal cats. There is no foundation for the statement that adrenalectomized rats succumb to a very much smaller dose of morphine than normal rats. C. G. L. W.

Stewart, G. N., and **Rogoff, J. M.** **The influence of muscular exercise on normal cats compared with cats deprived of the greater part of the adrenals, with special reference to body temperature, pulse, and respiratory frequency.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 87.

It is widely held that muscular weakness is a symptom of adrenal insufficiency, and often assumed that interference with the epinephrin output is the factor essentially responsible for muscular weakness. Normal cats and cats after removal of the greater portion of the adrenal tissues or interference with adrenalin production by section of the nerves, were subjected to prolonged and repeated spells of muscular exercises. No difference was made out as regards resistance to, or recovery from, fatigue, or as regards changes in rectal temperature, pulse, or respiratory rate. After severe muscular exertion a definite decrease of the adrenal content of an adrenal with its innervation intact, as compared with its previously denervated fellow, was observed, but only when the fatigue was excessive.

C. G. L. W.

Bolt, N. A., u. **Heeres, P. A.** Physikalisch-chemische Untersuchungen über die Bildung der Gallensteine. I. Der Einfluss der Zusammensetzung der Durchströmungsflüssigkeit auf die Geschwindigkeit der Gallenabsonderung und auf die Bildung von Gallenkonkrementen. [**Physico-chemical investigations on the formation of gall-stones. I. The influence of the composition of the perfusion fluid on the rate of bile secretion and on the formation of concrements.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 449.

The frog liver, when perfused with a modified Ringer's solution containing considerable amounts of bicarbonate, is stated to secrete bile which contains many cholesterol concrements. When colloids are added to the saline solution used for the perfusion, less 'bile' is secreted, and it is also found to be free from the concrements. The tendency to concrement formation is also reduced by the addition of lecithin to the perfusion fluid.

C. L. E.

Gellhorn, E. Beiträge zur vergleichenden Physiologie der Spermatozoa. II. Weitere Studien über Salzwirkung. III. Über Elektrolytgemische. [**The comparative physiology of the spermatozoa. II. Further studies on the effects of salts. III. On mixed electrolytes.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 555, 576.

II. Spermatozoa of the frog and guinea-pig show similar degrees of sensitiveness to a series of anions. Towards cations, with some variations here and there, it may be generally stated that the order of activity of a series is reversed in the two animals. The order of activity of the ions is similar to that for other physiological phenomena which are influenced by ions.

III. The effects on spermatozoa of one cation can be more or less neutralized by that of other cations; thus the effects of NaCl can be opposed by K, Sr, Mg, Ca, Ba, Fe, Pb. Similarly, the effects of the halogen anions can be overcome by phosphate, tartrate, acetate, and sulphate.

C. L. E.

Zwaardemaker, H. Über Fehlermöglichkeiten beim Vernehmen radiophysiologischer Untersuchungen. [**On sources of error in radio-physiological investigations.**] *Arch. f. d. ges. Physiol.*, 1922, **193**, 317.

The precautions to be observed in experiments on the frog's heart, rabbit's heart and intestine, the uterus, oedema, perfusion, and emanation experiments are detailed. C. L. E.

Redfield, E. S., Redfield, A. C., and **Forbes, A. The action of β-rays of radium on excitability and conduction in the nerve trunk.** *Am. J. Physiol.*, 1922, **59**, 203.

Observations on the frog's sciatic nerve show that peripheral nerves are very resistant to the effect of radiation. After intense radiation with β-rays there is loss of function which affects both conductivity and excitability. There may be a marked latent period between the termination of radiation and loss of function. Correlated with this loss of function there is an obvious physical change in the radiated nerve, which becomes stiff. Microscopic examination after treatment with the Marchi method shows, according to the authors, ' fatty degeneration of the myelin sheath '. [Note by abstractor: The microphotograph which accompanies the article is not a convincing proof of this last statement. It is difficult to believe that such a profound change, which in spite of various attempts has never been produced in nerves kept outside the body, and which, *in vivo*, in a warm-blooded animal takes several days to appear, can have been produced in a frog's nerve within the few hours of these experiments.] W. C.

Laskley, K. S. Studies of cerebral functions in learning. IV. Vicarious functioning after destruction of the visual areas. *Am. J. Physiol.*, 1922, **59**, 44.

The visual area in the rat, which is restricted to the occipital pole, is the only part of the cerebrum concerned with the performance of visual habits. Its destruction is always followed by loss of visual habits, while closely adjacent areas may be destroyed without affecting visual discrimination. The visual habits, lost by its destruction, may be reacquired rapidly. This capacity of the central nervous system for vicarious functioning in learning, which is not restricted to the visual area but holds good generally, raises the question whether or not its mechanism is based on cerebral localization. In order to test this question the visual area was destroyed in fourteen rats. These were then trained to discriminate differences of light intensity. When the habit was acquired a second operation destroyed some other cerebral area. Tests were then made to determine loss or retention of the habit after the second operation. The habit survived the destruction of any given third of the cortex left intact by the first operation. The only part of the cortex which remained unexplored was a small area in contact with the floor of the cranial cavity. It is certain, therefore, that there is no cerebral localization in vicarious functioning, at least so far as the visual area is concerned. W. C.

Roaf, H. E. Urochrome as a derivative of chlorophyll. *Biochem. J.*, 1921, **15**, 687.

Green parts of plants increase the output of urochrome in the urine, while carotene does not. It seems probable that urochrome is a derivative of chlorophyll. C. G. L. W.

RADIOLOGY

Radiotechnique

Voltz, F. Die physikalischen und technischen Grundlagen der Messung und Dosierung der Röntgenstrahlen. [**The physical and technical foundations of the measurement and dosage of X-rays.**] 1921, Urban, p. 300.

As the name implies, this book of 300 pages and 173 illustrations is an account of the physical and technical principles underlying the measurement of X-rays and their medical administration. It is complete in form, elaborate in detail, and contains a large amount of information, much of which should certainly prove of value as well as interest to the radiologist who desires precision in his work.

A brief introduction upon the general physical aspect of X-rays and their place in the spectrum leads to the more detailed development of Part II where all the variables concerned in the production of X-rays are separately considered and the object receiving the radiation then comes in for special consideration. How the dose of radiation received by a surface varies with the experimental conditions which may be met with in practice receives considerable attention.

Part III is divided into four sub-sections dealing with—

(*a*) The measurement of the quality, i. e. the wave-length of X-rays.

(*b*) The measurement of the quantity of X-rays.

(*c*) The measurement of the energy of the X-rays absorbed by an interposed object.

(*d*) A comparison of the methods employed for the measurement in question.

The whole contents of the book, which is mathematical in parts, will appeal more to physicists than to medical radiologists. Even so the radiologist will often be able to get information of a direct experimental character which will give him the answer to many a question which confronts him in the therapeutic application of X-rays to deep-seated growths.

It remains an urgent matter that an international unit of X-ray energy be adopted. This has been done in other regions of the electro-magnetic

spectrum and it is hoped that this question will soon receive due consideration, owing to the extended use of X-rays and the present difficulty of interpreting one arbitrary unit in terms of other equally arbitrary units. S. R.

Nadaud. Technique pour radiographies dentaires par pellicles intrabuccales. [**Technique for dental radiography by means of intrabuccal films.**] *J. de radiol. et d'électrol.*, 1921, **5**, 505.

The sizes of films used are 2 cm. × 3 cm. for a single tooth and 4 cm. × 3 cm. for more than one tooth. The method of packing the films and placing them in position in the mouth is described at length, and particular stress is laid on the direction of the normal ray. The method of making the exposure is described shortly. It is claimed that the technique gives clearer and more detailed results than any other. The criticisms of Jaugeas are replied to. In conclusion, the method is shortly compared with the external method and the intrabuccal method of Costa and Sinclair. P. L.-B.

Radiodiagnosis

Weill, E., et **Dufourt, A.** Sur quelques points de radiologie concernant les affections pleuro-pulmonaires de l'enfance. [**Some points in the radiology of pleuro-pulmonary conditions in childhood.**] *J. de radiol. et d'électrol.*, 1922, **6**, 1.

The paper chiefly deals with pneumonia and tuberculosis.

I. The pneumonic triangle. The authors make a *résumé* of the examinations of over a hundred cases of pneumonia in children in which it is stated that 'the pneumonic triangle is the rule'. The usual appearance of the triangle in pneumonia of the upper lobe is described in its various types according to the type of disease, and also when there is a pneumococcal septicaemia. After the crisis the last part to appear is the first to fade, and the last part to be seen is in the axillary area posteriorly. The radiological aspects in pneumonia are not always simple, for various reasons which are described. The appearance of the triangle depends on hepatization occurring first in the regions most remote from the hilum and occupying a vascular area; it indicates moderately intense thickening. In some cases, where the thickening is not so intense, there is only an indistinct shadow. The authors distinguish four types of pneumonia, (1) with an early triangle, (2) with a late triangle, (3) cases with no clinical signs and only revealed by the triangle, (4) cases with clear clinical signs unaccompanied by the triangle. These various types of pneumonia are discussed shortly, and also central pneumonia, in which the triangle occurs but may be obscured for 5 to 7 days. The late triangles differ from the early ones in most cases, the former being large and adjoining the supplementary shadows which alter the clearness of the outline. Generally speaking, the early triangle occurs in pneumonia of the apex, while the late triangle occurs in pneumonia of the base. The reasons for the anomalies in types 3 and 4 are discussed shortly. *The duration and date of disappearance of the triangle.* As a general rule there is no relation between the auscultatory signs and the triangle. The

triangle usually remains up to the crisis and fades gradually, but may have disappeared in twenty-four hours. The crisis always precedes the disappearance of the shadow, but does not necessarily bring it about, as the triangle may exist when there is no pyrexia or auscultatory signs. The significance of this fact is not stated. *Diagnostic value of the triangle.* The authors state that the triangle is of great diagnostic value: as regards differential diagnosis, in a case of pneumonia due to Friedlander's pneumobacillus there were only diffuse shadows, while definite tuberculous pneumonia can give rise to a triangle; differences in the latter case are described.

II. Shadows as transverse bands. The forms of the bands are described; they cut the pulmonary area into two parts. They vary greatly in size, from a handbreadth to the thickness of a finger. The authors state that their significance is not always clear, often they are found accidentally; they occur most frequently in tuberculous cases. If seen early they appear to be an outgrowth of the mediastinal shadow and resemble the 'duck's beak' shadow of Combes. The band increases in size and reaches the periphery in the axillary line. The authors believe that these bands are caused in the first place by the glands round the hilum, some of which are intrapulmonary. Usually the bands can be easily differentiated from the shadows due to interlobar pleurisy, which often has the shape of a biconvex lens.

Numerous radiographs and diagrams illustrate the points brought forward in the paper. P. L.-B.

Sinding-Larsen, C. M. F. A hitherto unknown affection of the patella in children. *Acta Radiol.*, 1921, **1**, 171.

The author describes at some length the clinical and X-ray signs of two cases in which a young girl complained of pain in one knee after strenuous exercise. Clinically the lesion was one-sided, but radioscopically the other patella was seen to be affected. In both cases the affection disappeared in about four months with little or no treatment. The author considers the affection to be a simple traumatic periosteal or epiphyseal irritation. Nine skiagrams accompany the paper. P. L-B.

Abrahamsen, H. Koehler's disease, especially with a view to the pathogeny of the same. [B.] *Acta Radiol.*, 1921, **1**, 173.

The author starts by describing the symptoms, and states that a correct diagnosis can only be made by means of X-rays when a diminished, condensed centre of ossification is found in the navicular bone or the centre is formed of islets and the edges are frayed. A case is described in which the centre of ossification in the navicular was almost missing. The various views as to the pathology of the disease are shortly gone into, and the author agrees with Koehler that the disease is an anomaly of development and thinks that his case supports this view. He does not attempt to say where the cause of the anomaly is to be found. Radiographs accompany the paper. P. L.-B.

Henrard, E. Extraction des corps étrangers de l'œsophage et des voies aériennes supérieures. [**The extraction of foreign bodies from the oesophagus and upper air-passages.**] *J. de radiol. et d'électrol.*, 1921, **5**, 436.

The author claims 100 per cent. success for his method, but says that it has always been ignored by laryngologists. Various accidents and disasters (of which ten that came under his own observation are mentioned) have led him to recall attention to his method once more. He asserts that these accidents and the encouraging results obtained by other methods than use of the oesophagoscope or bronchoscope allow conclusions to be drawn as to the management of a case in which a foreign body has entered either the oesophagus or upper air-passages. Before oesophagoscopy or bronchoscopy the patient should be examined under the X-rays, and if this be negative, or the foreign body be not opaque, other methods are adopted. The two great classes of foreign bodies opaque to X-rays are those of the type of a coin and those such as a denture, which can stick into the oesophageal wall. The great majority of the first type lodge at the narrowing of the oesophagus caused by the cricoid and can be easily extracted under the screen by the method described by the author in March 1907; this is claimed to be easier and quicker than using the oesophagoscope. A short description is given of the method of removal of coins from various situations in the oesophagus; this is followed by a tabulated list of 55 cases of foreign bodies in the oesophagus, 52 of which are at the level of the cricoid. Dufourmontel's paper to the Paris Congress of Surgery in October 1920 is quoted on the difficulties of extracting dentures. Three other authors who extracted foreign bodies in difficult cases under the screen are quoted, and the author states that Kermisson's curved forceps used under the X-rays are superior to the oesophagoscope. He then describes the methods of removing foreign bodies which stick into the oesophageal wall at various levels. The paper is concluded by a short account of the technique for removing foreign bodies from the upper air-passages. P. L.-B.

Radiotherapy

Perthes. La radiothérapie des tumeurs malignes. [**The radiotherapy of malignant tumours.**] *J. de radiol. et d'électrol.*, 1922, **6**, 122.

The author favours in most cases a combination of X-rays and radium. In cases of cancer of the breast, stomach, and intestine he believes that in operable cases operation should be performed as soon as possible, but perhaps this may be modified in rectal cases on the lines of Chaoul's treatment. In breast cases prophylactic irradiation should be carried out after operation. Cancer of the uterus, he states, is the most favourable type for radiotherapy. A short reference is made to the benefits of X-ray therapy in inoperable cases, which may then sometimes become operable. Treatment of post-operative recurrences, particularly in breast cases, by X-rays is stated to be of great use.

In the case of X-ray therapy of sarcomata the author refers to the work of Jungling and puts forward the most important of his conclusions: (1) Lymphosarcomata react well, but extension to neighbouring glands

usually occurs. (2) Periosteal sarcomata of the head of long bones or neck of the scapula should be treated by X-ray therapy, as the results of operation are always bad. (3) In myeloid sarcomata, if it be a question of amputation, X-rays should be tried. (4) X-ray therapy has given good and lasting results in osteo-sarcomata of the skull. (5) Radiotherapy has not given good results in cases of sarcoma of the superior maxilla; operable cases should be operated upon. (6) In all inoperable cases X-rays should be tried. The author believes that gliosarcomata of the brain should also be treated by X-rays, and that the effects of hypophyseal tumours can be benefited by the same treatment. Tumours whose nature as to malignancy is uncertain, such as fibrous tumours of the nasopharynx, the author believes should be irradiated. A short reference is made to the dangers and inconveniences of radiotherapy.

It is then stated that the essential task of the radiologist is to expose every part of the body harbouring malignant cells to a lethal dose, and the author asks: Is there a cancer dose, and do all the types of malignant cells in different persons react the same under X-rays? In answer to the first part of the question, he states that there is no such thing as a cancer dose in the sense of one that will without doubt bring about the regression of a cancer; as regards the second part he states that malignant cells differ in radiosensibility, particularly in the case of sarcomata. Tumours histologically similar may react very variably to irradiation, and, further, cells at the centre and periphery of the same tumour differ in their radiosensibility: the problem is a biological one, not purely physical. The author believes that the best results are produced by a single irradiation, giving a heavy dose.

He believes that the chief effect of the rays is to destroy the power of division in the neoplastic cells, and that a dose less intense than is necessary to bring this about becomes a stimulant to division. In the X-ray therapy of cancer, in his opinion, there are two factors; on the one hand the attack on the malignant tissue, and on the other the active co-operation of the surrounding healthy tissue; care must be taken not to nullify the latter by too heavy a dose. P. L.-B.

Riedel, G. Über kombinierte Sonnen- und Quarzlichtbehandlung bei Knochenerkrankungen, insbesondere bei chirurgischer Tuberkulose unter Berücksichtigung des Blutbildes und seiner Änderung. [B.] [**On the combined sunlight and ultra-violet treatment of joint diseases, especially surgical diseases, with special reference to blood changes.**] *Strahlentherapie*, 1921, **12**, 361.

This is a long paper on the subject of the combined sunlight and ultra-violet treatment of joint diseases, especially of surgical tuberculosis. A comparatively small portion of the paper is, however, devoted to the cases treated, for no less than 17 pages have to be read before we come to the author's own investigations. These pages, with the voluminous bibliography, which contains about one hundred and fifty references, should, however, be valuable for general purposes of reference.

Details are given of the treatment of about 50 cases, with the blood changes observed during this period; this section is then followed by a discussion on the part of the author as to what the most salient features

are in these blood changes—the haemoglobin, the red corpuscles, the colour index, the leucocytes, all come in for consideration. The effect upon pigmentation processes is one of considerable interest, for it has been frequently reported from alpine sanatoria that the failure on the part of the patient to pigment when exposed to ultra-violet radiation is an indication that this form of therapy is not likely to be of use. It is, however, not yet proved that there is any causal relationship between these two findings, but the degree of pigmentation is variable among patients all receiving the same radiation, and it still remains a problem as to how this pigmentation is brought about. The article, though not largely concerned with entirely new methods, is a valuable one, and comes from the University Clinic for Orthopaedic Surgery at Frankfort on the Maine. S. R.

Radiobiology

Nakahara, W., and **Murphy, J. B. Studies of X-rays effects. X. The biological action of small doses of low frequency X-rays.** *J. Exper. M.*, 1922, **35**, 475.

The authors state that attempts to compare the biological action of soft and hard rays were of little value owing to the apparatus and measuring devices at their command, but it appeared definite that by using the softer rays it is possible to induce a stimulation of the lymphoid cells which is preceded by only a very short and transitory depression. The first satisfactory results were obtained with a spark-gap of about $1\frac{1}{2}$ inches; later, $\frac{7}{8}$ inch was used with a better result. In the present paper still softer rays were used, generated from a special water-cooled tube with a window of thin glass which allows the passage of the rays usually held back by the standard tubes.

Production of lymphocytosis. A description of the experiment made to determine the time of exposure necessary to produce a maximum stimulation of the lymphoid tissue in mice is described. From this it was found that 1 minute was the necessary time. Counts were then made on 30 mice which were afterwards radiated for 1 minute; counts were made at intervals afterwards. From this it appears that the absolute number of polynuclears does not alter appreciably, but the lymphocytes increased considerably, being almost doubled on the second day, and remained increased on the eighteenth day. The initial depression is not dealt with.

Histological changes. The material was collected from 26 mice irradiated as a parallel experiment to the above: the animals were killed in groups—24 hours, 4, 7, 10, and 14 days after exposure—and various tissues removed and fixed in Carnoy's fluid. *Lymphoid organs.* Changes in the spleen and lymph glands were almost identical. There was no change after 24 hours. In 11 mice killed on the fourth and seventh days the mitotic figures were very numerous: those killed on the tenth and fourteenth days showed that the proliferative activity was almost normal again. *Suprarenals.* These were reddish in colour and enlarged. The sinus-like spaces between cortex and medulla were distended with blood and also the capillaries

between the cortical cell columns. There was no necrosis. This vascular change was seen in all mice except those killed after 24 hours. *Other organs.* No changes were seen, even in the germ cells of the ovaries and testes.

Effect on resistance to transplantable cancer. Reference is made to the fact that a small dose of X-rays, sufficient to stimulate the lymphocytes, increases the resistance of rats and mice to transplanted cancer. From the experiments carried out it is seen that there is no evident immunity when the inoculation is made 3 days after X-raying. Of mice inoculated 7 to 14 days after treatment 34·4 per cent. were immune, and of those treated 10 days after inoculation 42·8 per cent. were immune.

The absorption coefficient of X-rays produced by a voltage measured by a ½ inch spark-gap. The very soft rays produced by a voltage measured by a ½ inch spark-gap are practically homogeneous, with a mass absorption coefficient equal to 3·4 for water: this includes the mass-scattering coefficient as 0·2. The value was measured photographically. The method of comparison is fully described.

The paper concludes with a short discussion and summary.

P. L.-B.

Murphy, J. B., Heng Liu, J., and **Sturm, E. The action of serum from X-rayed animals on lymphoid cells *in vitro*. The effect of the serum from animals after a very large dose of X-rays on lymphoid cells.** *J. Exper. M.*, 1922, **35**, 382.

The question before the authors was whether the serum of X-rayed animals has any effect on lymphoid cells *in vitro*. Rats were used for the investigation in view of the known susceptibility of their circulatory lymphocytes; the animals were exposed to X-rays from a 'soft' bulb, spark-gap 2½ inches, milliamperes 10, anticathode animal distance 12 inches, time 14 minutes. Immediately after the exposure the rats were anaesthetized and exsanguinated by aspiration of the heart; serum was then collected. Normal rats were similarly dealt with, and from them the thymus and mesenteric lymph glands were aseptically removed. These glands were divided into equal parts, one portion being mixed with serum from the normal rats and the other with the serum from the irradiated ones. The suspensions were passed through filter-paper under suction to remove fibrous tissue and cell clumps. Counts were made of the two filtrates and then enough sera added to reduce them to between 10 and 20,000 cells per c.mm. They were then placed in a water-bath at 37° C. for 2 hours and counts remade. The average of fourteen experiments showed that whereas the cells suspended in normal serum decreased, those in the serum from X-rayed animals showed an approximately equal increase. Repetition of this experiment in which the serum was X-rayed *in vitro* failed to show any such difference. The authors are inclined to attribute this difference to the stimulating substance being a disintegration product of lymphoid cells, present under the first but absent in the second experimental arrangement.

S. R.

Lawrence, R. D. The effect of X-rays on enzyme action. *Arch. radiol. & Electroth.*, 1922, **26**, 244.

The views on this subject are very varied at the present time. The author reviews shortly the work of Richter and Gerhartz, who thought the effect was negative, and Richards, who thought there was a slight but constant effect. In the author's experiments the blood diastase and urinary diastase were used. Wohlgemuth's method of estimating diastase was used throughout and is described. Radiation was carried out with a Coolidge tube; distance from the anticathode 9 inches; $5\frac{1}{2}$-inch gap and unfiltered radiation at 2 milliamperes in the secondary. In every experiment radiation was found to have no effect, so the author concludes that even if there be any effect it is extremely slight and of no practical importance.

P. L.-B.

MEDICAL SCIENCE

ABSTRACTS & REVIEWS

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All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [*B*] *after the title signifies that the original memoir contains a good bibliography of the subject dealt with.*

REVIEWS

RENAL DISORDERS

Symptomatology. Parmenter, instructor in hygiene at Harvard University, examined 513 freshmen during the college year whose average age was 18. 40, or approximately 8 per cent., showed **albuminuria.** Examination of the sediment showed nothing more than an occasional cylindroid or a few squamous cells. Six of the 40 were excluded as having organic disease which might account for their albuminuria. In the second examination some weeks later, 16 of the 34 persisted in showing albuminuria, and at a third examination a fortnight later albuminuria was still present in 6. Thus approximately 5 per cent. had a transitory albuminuria which might be designated as functional. The 6 men who showed albuminuria on repeated examination were found to have it only in the specimens taken during the day and never in the morning specimens. In the routine physical examination, these 6 men had been classified as D, i. e. as having a very poor standing posture and very poor mechanical use of the body.

Saito, of Nagasaki, investigated 44 children who showed a moderate or severe degree of orthostatic albuminuria with the following results: (1) 14 had nervous diseases such as chorea, periodic vomiting, asthma, and enuresis, and the other 30 complained of nervous disturbances such as headache, weariness, and palpitation; lordosis of the lumbar spine was found in 55 per cent.; (2) tuberculosis and syphilis had no bearing on the condition; (3) the great majority of patients (70 per cent.) with orthostatic albuminuria were in a state of vagotonia; (4) renal function as measured by the phenol-sulphonephthalein test was generally normal; (5) the blood-picture was characterized by pseudo-anaemia, eosinophilia, and occasionally leucocytosis; (6) the amount of the acetic acid body in the urine varied either absolutely or relatively even in the same individual; (7) the albumin quotient of the proteids in the urine was equal to that of the serum and of the cerebrospinal fluid; (8) the most reliable methods for provoking albuminuria were (*a*) to make the individual hold a rod at the level of the shoulders for 10 minutes, and (*b*) to make him kneel down for 10 minutes; (9) the direct cause of albuminuria may be lordosis of the lumbar spine. Albuminuria, however, does not occur merely with lordosis, and vasomotor instability is also probably a factor.

According to Harrison, true proteinuria probably never reappears in the recumbent position in cases of cyclic proteinuria. If proteinuria does recur while the patient is lying in bed, an organic lesion should at once be suspected. The albuminuria of a small organic kidney lesion may be postural in type, i.e. the amount of protein may fluctuate in organic albuminuria so as to simulate a condition of functional cyclic albuminuria. In the latter

condition, however, once the protein has disappeared from the urine as the result of lying down it probably never reappears while the ordinary recumbent position in bed is maintained. Harrison thinks it possible that in certain cases of mild organic disease of the kidney (or other part of the urinary tract) the proteinuria is postural in type simply owing to the drainage of foci of disease in the erect posture. The fact that in postural proteinuria the 'albumin' may appear, then disappear, and later reappear, the erect posture being maintained throughout, should make us very sceptical of so-called cures by any particular drug, such as calcium lactate, &c.

Maclean remarks that though the albuminuria of adolescents is well known it is not generally recognized that albuminuria apart from kidney disease is by no means uncommon in adults between 20 and 45 years of age. As the result of an examination of over 60,000 soldiers for albuminuria and casts, Maclean found that the actual incidence of albuminuria of all kinds was 6·48 per cent. After allowance had been made for cases with pus, spermatozoa, &c., the general incidence of albuminuria was 5·62 per cent. Roughly speaking, therefore, about 5 per cent. of the men examined had some degree of albuminuria which could not be accounted for by the presence of pus or other substances. About 2 per cent. of these had very well marked albuminuria. The average number of albuminous urines found to contain casts was 1·87 per cent.; of these 0·84 per cent. had definite epithelial casts, and in 1·03 per cent. hyaline casts only were found. Maclean states that though albuminuria is present in many cases of renal disease, in many other cases, which are sometimes of a severe nature, it is never found. On the other hand it is undoubtedly true that the majority of patients who have albuminuria are not suffering from any defect of the kidneys, and are not more likely than any other average individual to do so in future. To ascertain in any given case whether or not albuminuria is important, certain renal tests must be applied, the simplest of which is the urea concentration test of Maclean and De Wesselow (vide *Medical Science*, 1920, **3**, 122).

Datta, of the Turin Pathological Institute, records 3 cases of **paroxysmal haemoglobinuria** in patients aged 49, 24, and 34 respectively. The Wassermann reaction was positive in all, although in two there was no history or other evidence of syphilis. Both spontaneous and provoked attacks became less frequent, and disappeared entirely under treatment by salvarsan or neosalvarsan. Clinical improvement was accompanied by attenuation and complete disappearance of the positive Wassermann reaction.

Bondy and Strisower record two cases of haemoglobinuria due to cold treated by intravenous injections of hypertonic saline solution with temporary improvement. The doses ranged from 60 to 170 c.cm. The Wassermann reaction was feebly positive in one and negative in the other. Examination of the blood showed an increased resistance and a fall in the number of the red cells in both cases after the injection. Immature nucleated red corpuscles were not observed. An increase of the leucocytes, especially the polymorphonuclears, was almost always found. On the other hand, Kaznelson, of Prague, used the method of Bondy and Strisower in two cases of paroxysmal haemoglobinuria without observing any effect upon the attacks. Three injections of milk in one of his cases were equally unsuccessful.

Schiassi, in an article on paroxysmal haemoglobinuria, comes to the following conclusions:

1. In a classical attack of paroxysmal haemoglobinuria provoked by cold bathing, there were observed a marked diminution in coagulation time of

the blood and an evident leucopenia, followed as a rule by leucocytosis. In even incomplete attacks leucopenia was constant.

2. By reducing the degree of cold one was able to produce incomplete paroxysms (lacking haemoglobinuria), and of these the chief symptoms were leucopenia, nausea, and fever.

3. One was not able to produce on the same day a second paroxysm, notwithstanding the presence of haemolysin and complement, because the first experimental attack produces a desensibilization to the action of cold. We must therefore add to the series of anaphylactic phenomena that of desensitization to the action of cold, which is to be classed with those enumerated by Micheli (fever, nausea, pain), and by the French school (leucopenia, variations in the coagulation power of the blood).

4. The acute renal lesion which follows an attack of haemoglobinuria is not properly or accurately described as due to the blocking of renal tubules by 'granular detritus', since the material in question is formed wholly from haemoglobin.

5. The patient was subjected to a course of treatment for syphilis and has not had an attack of haemoglobinuria during the five years which have elapsed.

Bittorf, of the Breslau University Medical Policlinic, remarks that though the occurrence of haemorrhagic nephritis in convalescence from acute nephritis is well recognized, very little is known of attacks of haemoglobinuria under the same conditions. He has recently seen three cases of this kind in patients aged between 20 and 45, two of whom had had war nephritis, and one was a woman who had acute haemorrhagic nephritis. There was no sign of syphilis in any case, and the Wassermann reaction was negative in all. None showed any trace of haemoglobinaemia, so that the haemolysis must have occurred in the kidney.

Walters reports three cases in which **Bence-Jones proteinuria** was observed. The first case had at no time symptoms referable to the osseous system except anaemia, the second case is assumed to have been one of generalized carcinomatosis, and the third was a classical case of multiple myeloma. None appear to have come to autopsy, but the clinical details are meagre and unsatisfactory. Certain experiments were made on the metabolism of the protein, and the following facts elicited: (1) The output of Bence-Jones protein is independent of the protein intake, of the time of day or night, and of the total urinary nitrogen; (2) the Bence-Jones protein was isolated from the blood plasma and also from bronchial secretions; (3) it was absent from the cerebrospinal fluid and saliva.

Schirokauer, of the Third Medical Clinic of Berlin University, inquired into the subsequent history of 26 of the worst cases among 200 patients with **war nephritis** who had contracted the disease on the Western Front in 1917. He learnt that two had died in 1919, and of the remaining 24 the urine was free of albumin, and showed nothing abnormal in the sediment in 22. The circulatory organs were normal in almost all the cases, only two elderly persons, probably from other reasons, having a blood-pressure of 140 mm. Hg. In one case there was only a trace of albumin, and a few red cells in the urine, and in another the albumin content of the urine ranged from 1 to $1\frac{1}{2}$ per mille. In neither case was the blood-pressure raised. Schirokauer considers that the 22 other cases, who were following their ordinary occupations, were cured. Even supposing that only 22 of the 200 cases or 11 per cent. could be regarded as cured, these results are about 3 times as

good as those of Schlayer, who reported that only 4·4 per cent. of his 135 war nephritis cases ended in complete recovery (vide *Medical Science*, 1920, **3**, 121). Schirokauer concludes that the prognosis of so-called war nephritis under proper treatment is as favourable as that of acute nephritis in peace time.

Deutsch, of Vienna, examined 200 men who claimed a pension for war nephritis. The majority dated the beginning of their disease from the years 1916 or 1917. Almost twice as many were between the ages of 30 and 40, as between 20 and 30. In the former group the disease had been at its height in 1917, and in the latter in 1916. 99 or 49·5 per cent. could be regarded as completely recovered, 43 or 21·5 per cent. as incompletely recovered, and 58 or 29 per cent. as not recovered. A long stay in hospital did not appear to have had any effect upon the final issue of the disease. 29 per cent. were considered to be entitled to a pension, but in over 60 per cent. of these the disability was estimated at not more than 20 per cent.

As a thorough examination of the renal function was not practicable, the examination of applicants for a pension was limited to determination of the blood-pressure and investigation of the heart (clinically and by X-rays) and vascular system in those cases in which the urine showed nothing abnormal in the specific gravity or the sediment, and in which the history was not at variance with a negative urinary finding. In all doubtful cases concentration and dilution tests were also employed. Those cases were regarded as completely recovered in which no morbid changes were found either in the urine or the cardio-vascular system, while those in whom the renal function was found satisfactory, but the blood-pressure and vascular system showed definite deviations from the normal, were regarded as incompletely recovered. Cases were classified as 'not recovered' in which the urine contained more or less albumin and blood in association with corresponding symptoms of renal disease.

Major, of the Henry Ford Hospital, Detroit, records a case of **chromic acid nephritis** in a man aged 59, who was being treated by applications of chromic acid crystals for carcinoma of the cheek. No oedema was noted clinically, and no anasarca or ascites was present at the autopsy, which showed that the lesion was a pure tubular nephritis. No symptoms of uraemia were present, and the patient during the greater part of his illness felt comparatively well. The urine output after a temporary depression was high, but the urine itself was of low specific gravity, and the excretion of nitrogen, chlorides, phosphates, creatinin, uric acid and urea was markedly diminished.

According to Epstein, of New York, **chronic nephrosis** is a very frequent condition possessing the following characteristics. The disease occurs in relatively young persons. It is of obscure or unknown origin and bears no definite relation to known infectious diseases. In some instances pregnancy may be related to it aetiologically. It is characterized clinically by a gradual onset, protracted course, oedema, anasarca, and effusion into the serous cavities; by oliguria, pronounced albuminuria with or without casts, and a high specific gravity. It is also characterized by absence of any increased blood-pressure and any cardiac hypertrophy, and by the absence of any marked nitrogen retention in the blood. Lastly, its fundamental characteristic is a marked increase in the cholesterol content of the blood, a reduction in the total protein of the blood serum, and the inversion of the normal ratio of albumin to globulin. Epstein regards chronic nephrosis as a metabolic disease allied to states of hypothyroidism, and has therefore, in addition to

the dietetic treatment previously described (vide *Medical Science*, 1920, **3**, 126–7), used thyroid gland therapy in a number of obstinate cases with gratifying results.

J. H. Barach, of the Presbyterian Hospital, Pittsburg, states that *nocturnal polyuria*, or the passage of more urine during the night hours than during the day, is a highly diagnostic symptom of an established subacute or chronic nephritis, and occurs independently of arterial hypertension. In all points except the higher concentration of urea during the day hours, the night urine presents the characteristics of the day urine. Barach's observations showed that the nocturnal polyuria was not the result of heavy evening meals, physical exertion, arterial hypertension, or the horizontal posture. The most probable cause seemed to be found in the physiological adjustments in circulation incidental to sleep. Barach concludes that noctural polyuria is primarily a manifestation of increased elimination of water because of a more favourable state of the renal circulation, and that the increased elimination of salts is coincidental rather than causative.

Cornell, of Brockville, Ontario, has found from a study of more than a hundred cases of chronic nephritis that various degrees of a *dyspnoea* occur which is distinguished from cardiac dyspnoea by the absence of cyanosis and the readiness with which it is cured by administration of sodium bicarbonate by mouth. The detection of acidaemia is therefore of diagnostic and therapeutical importance. A syndrome of lumbar pain, frequent micturition, and dyspnoea of non-cardiac origin is suggestive of incipient nephritis, even in the absence of albuminuria. Non-cardiac dyspnoea is a very early symptom in nephritis, and has frequently led Cornell to prolong the search for albumin with ultimate success, although albuminuria was absent as long as two weeks.

According to Alwens and Moog, of the Frankfort University Medical Clinic, **involvement of the heart** is the rule in the initial stage of acute nephritis. An exact demonstration of a cardiac lesion can only be obtained by X-ray examination, the condition at this stage being probably a continuation of hydro-pericardium with acute dilatation of the heart. As a rule it rapidly subsides at the same time as the other symptoms of dropsy and backward pressure in the internal organs. Hypertrophy of the left ventricle does not occur until after several weeks, and appears to coincide with the passage of the disease into the subacute or chronic stage.

A. L. Barach, of the Medical Clinic of the Presbyterian Hospital, New York, gives a description of 30 cases of chronic nephritis in patients aged from 15 to 57, complicated by acute pericarditis. The conspicuous features of the cases were a marked nitrogen retention in the blood, a constantly present acidosis, a high blood-pressure, severe secondary anaemia, and a tendency to haemorrhage (petechiae of the skin and mucosae, epistaxis, haematuria, and rectal haemorrhages). The pericarditis was not a terminal complication, as the average duration of life after the onset of the pericarditis was 29 days. Excluding one patient, who lived one year thereafter, the average figure was 16 days. Death in many cases was due to retention of nitrogen in the blood rather than to advancing heart failure and acidosis. In four cases direct culture of the pericardium yielded pyogenic organisms, while in four other cases cultures of the pericardium were sterile. Barach holds that the majority of cases of pericarditis in chronic nephritis are of non-infectious origin, and are due to a chemical irritant, and that only

a small group are due to frank infection of the pericardium. He admits, however, that the inflamed pericardium may sometimes become secondarily infected.

Having observed that the **blood-pressure** in the various forms of Bright's disease was liable to periodical variations in the course of the day, Kylin measured the arterial blood-pressure morning and evening with Riva-Rocci's sphygmomanometer. In order to obtain an independent idea of the physiological variations of the blood-pressure, observations were first made on 10 patients who showed no evidence of renal or vascular disease. The blood-pressure charts of these patients presented only slight changes from day to day, and never exceeded 5–10 mm. Hg. The morning readings were, as a rule, lower than those in the evenings. In mild nephrosclerosis, on the other hand, the blood-pressure charts were quite different, the daily changes being as much as 50 mm. and more. The greatest difference noted within 24 hours was 75 mm. Hg. In these cases also the readings were usually lower in the morning than in the evening. Kylin thinks that these great variations can only be explained by a functional constriction in the vascular system. According to some, the primary factor is renal disease, while others maintain that the hypertonus is primary and that the renal disease is a result of the hypertonus. In acute glomerulo-nephritis the behaviour of the blood-pressure was quite different from that in mild nephrosclerosis. In some cases of acute glomerulo-nephritis the rise of blood-pressure was considerable and in others only slight. The variations from day to day were relatively small, although they were greater than under physiological conditions.

Flurin, of Cauterets, maintains that each of the three principal syndromes of Bright's disease, viz. the cardio-vascular syndrome, the syndrome of chloride retention, and the syndrome of nitrogen retention, is associated with a special form of **rhinopharyngitis**. In the cardio-vascular syndrome or syndrome of hypertension, hyperaemia of the pharynx is often the first sign of Bright's disease. The mucous membrane is congested and varies in colour from a bright red to a deep carmine, the usual colour being a uniform raspberry. The mucous membrane is also thickened and swollen, and covered with viscid mucus. The characteristic feature of the syndrome of chloride retention is oedema of the pharynx, which often accompanies or precedes anasarca. The uvula is chiefly affected, but sometimes one or both of the palatal arches may be involved. In some cases the oedema is preceded by a stage of infiltration in which there is a hypersecretion of all the glands to compensate for the renal insufficiency, rhinorrhoea and bronchorrhoea being particularly abundant. In addition to those two forms, an apparently ordinary rhinopharyngitis may develop either at the onset or at an advanced stage of Bright's disease. In the syndrome of nitrogen retention Flurin observed a case in which the pharyngeal mucosa was dry and polished, deglutition was difficult, and the patient complained of a feeling of smarting in the throat. Although this was only an isolated instance, similar cases will very probably be observed when the pharynx is systematically examined in Bright's disease with nitrogen retention.

Bierry, Rathery, and Bordet emphasize the frequency of **hyperglycaemia** in severe chronic nephritis, but point out that rise in the proteid sugar is of much greater importance than increase of free sugar. Persistence of proteid sugar apart from any transitory acute attack always appears to be the sign of a fatal issue within a short time.

According to Mounier, in addition to the two types of **muscular uraemia** hitherto described, viz. the types with contractures and the paretic type, there is a myoclonic form, of which he records an example, characterized by the existence of involuntary muscular jerks and severe pain on pressure of the muscles. Mounier maintains that muscular uraemia, and especially the myoclonic form, indicates an extremely severe and intense auto-intoxication.

According to Kaulen, of the Cologne University Children's Clinic, who records two examples in children aged 5 and 9 years respectively, **skin haemorrhages** in chronic renal diseases and uraemia have rarely been described, though instances have been published by Ascoli, Bartels, Munk, Volhard, and others. No examples, however, have hitherto been reported in children. Although the possibility of these haemorrhages being due to obstruction cannot be excluded, the microscopical examination made in Gruber's case and one of Kaulen's show that the haemorrhages are due to inflammatory vascular changes.

According to Curschmann, of the Rostock University Medical Policlinic, who records a case in a woman aged 45, **paranephritic abscess**, so far from being a rare disease, is the most frequent of all metastatic staphylococcal affections. Its apparent rarity he attributes to the probability of many of these cases dying of 'cryptogenic sepsis' or 'typhoid fever', while a smaller number recover without operation or spontaneous evacuation of the abscess, which becomes encapsuled and desiccated instead. Most of the 18 to 20 cases which Curschmann has seen had been mistaken for typhoid fever at the height of their illness. The possibility of paranephritic abscess should therefore be considered in all obscure febrile diseases. In all such cases investigation should be made for boils, carbuncles, or whitlows, as well as for other sources of infection, such as the tonsils or the gums. The renal area should be explored by comparative inspection, palpation, and percussion on both sides, as well as by X-ray examination.

Bugbee remarks that while a hypernephroma is a frequent occurrence, a true **malignant neoplasm of the kidney** is relatively rare. Albarran and Imbert, in 1903, found only 13 examples of malignant adenoma out of 529 cases of renal tumour, and among 83 malignant tumours of the kidney operated on at the Mayo Clinic up to July 1, 1912, only 32, according to Braasch, presented the complete symptomatology of malignant renal tumour, viz. palpable tumour in the region of the kidney, persistent pain in the region of the tumour, haemorrhagic urine, and the general symptoms of malignancy. Two of the three symptoms were present in 37 cases, and only one in 14 cases. The clinical diagnosis, therefore, must often be based on only one or two cardinal symptoms. The conditions most likely to be confused with renal tumour are, (1) 'essential' and nephritic haematuria, (2) retroperitoneal tumour, (3) bilateral cystic kidney, and (4) closed pyonephrosis. In the great majority of cases a pyelogram clears up the diagnosis. Bugbee records a personal case in a man aged 44 of medullary carcinoma of the left kidney in which infection and nephrolithiasis probably played a part in the aetiology.

Comrie, in a consideration of the various **renal efficiency tests** comes to the following conclusions: (1) The combination of the estimation of blood urea, of urea concentration in the urine, and of phenolsulphonephthalein excretion gives reliable information as to the functional efficiency of the kidneys. (2) The blood urea estimation should form a preliminary investigation. If it rises above 50 mgm. per 1,000 c.cm. of blood, the condition is

serious. If it is persistently over 100 mgm., recovery is unlikely, and death will probably occur within a year. In uraemia it may exceed 200 or 300 mgm. before death. The blood urea may be normal, while a marked degree of renal impairment exists, but in such cases the immediate prognosis is usually favourable. (3) The blood-pressure shows no constant relation to the amount of blood urea, though when blood urea is permanently high the blood-pressure is usually high. (4) The phenolsulphonephthalein test is the most valuable individual test. An excretion which takes place chiefly in the first hour and in two hours reaches 70 per cent. or over is of good prognosis. An excretion of 50 per cent. for two hours, in either renal or cardiac cases, is compatible with complete restoration of health. An excretion of about 30 per cent. is compatible with prolonged life, though on a low plane of vitality. When the excretion does not rise about 20 per cent. in spite of treatment, death within a year may be expected. (5) The urea concentration test is simple, harmless, and gives valuable information. The amount fluctuates more in individual cases than does the phenolnephthalein excretion. A urea concentration over 3·5 per cent. indicates a satisfactory renal function; over 2 per cent. it is compatible with a fair degree of health; if it persists below 2 per cent. in spite of treatment it is unsatisfactory.

According to Fromm, the renal test meal consists of a definite carefully composed dietary régime of 24 hours' duration, consisting of three meals. It contains approximately 13·5 gm. of nitrogen, 8·5 gm. of sodium chloride, 1,760 c.cm. of fluid, and a considerable quantity of purin material in the form of meat soup, tea, and coffee. All these substances act as diuretics, and it is on the mode of excretory response to such stimuli that the interpretation of the test depends. The test-meal yields the following distinctive results in the different types of renal disease: (1) Chronic interstitial nephritis. In early cases nocturnal polyuria is usually the first sign of impairment. In advanced cases the following factors indicate renal insufficiency: (*a*) marked fixation and lowering of the specific gravity; (*b*) diminished total output of sodium chloride and nitrogen; (*c*) a tendency to total 24-hour polyuria; (*d*) a night urine showing an increase in volume, lowering of the gravity, and a concentration of nitrogen under 1 per cent. (2) Chronic parenchymatous nephritis. The characteristic findings in these cases are as follows: (*a*) the specific gravity tends to be high and fixed; (*b*) there is a diminished output of sodium chloride and water; (*c*) nocturnal polyuria is present; (*d*) there is a practically normal nitrogen excretion. (3) Renal congestion resulting from cardiac decompensation. The test meal is followed in such cases by the following effects: (*a*) a fixation of gravity about the level of 1020; (*b*) a diminished output of sodium chloride; (*c*) a diminution in the amount of the day urine; (*d*) a normal elimination of nitrogen; (*e*) a normal night urine.

According to Gram, Strauss's water test of the functional capacities of the kidneys has been carried out for several years at the Rigshospital in Copenhagen. The patient is given a litre of water between 6.30 and 7 a.m., and for the rest of the day he is kept on a dry diet. The urine passed at 6.30, 7, 8, 9, 10, and 11 a.m., and at 2, 5 and 8 p.m., as well as 5 a.m. next day, is measured separately. In health almost all the litre of water is excreted in the period 7–11 o'clock. The results of this test in orthostatic albuminuria depend largely on whether the patient is up or in bed. Among 6 patients with orthostatic albuminuria, the excretion of urine in the period 7–11 o'clock ranged from 908 to 1,578 c.cm., with an average of 1,173 c.cm., while

the patients were in bed. But when they were up, the urine ranged from only 208 to 842 c.cm. in the same period, with an average of 578 c.cm. Thus the excretion of the urine was reduced by more than 50 per cent. by the upright position. The reverse effect of posture on the excretion of urine was observed in 2 cases of nephritis which had reached the stage when the nephritic albuminuria has an orthostatic character. Gram accordingly suggests that this difference may prove a useful test for distinguishing between the albuminuria of nephritis and orthostatic albuminuria.

The effect of high protein diet on albuminuria and blood urea in cases of nephritis was investigated by Wordley, who found that variations in the amount of protein in the diet had no effect on the amount of protein excreted in the urine. Examination of the amount of protein excreted at different times of the day showed that it was subject to wide variations. It appeared to be lower in the urine secreted during sleep. It was found that the blood urea varied very considerably with the diet, and that an estimation of the blood urea was of much less value in appraising the impairment of the kidney function than Maclean's new urea test, as the blood urea might be within normal limits and yet all the manifestations of uraemia be present.

Rabinowitch, of Montreal, claims that there is no single test for renal function which can be used for the purpose of renal diagnosis to the exclusion of all others. He maintains that the information obtained from the simple nocturnal urine test parallels that obtained from the urea concentration test, but that both tests give only qualitative information. A correlation with the clinical picture is of paramount importance for the proper interpretation of any test.

Prognosis. James, of the Harvard University Medical School, has examined 70 children who had nephritis in the Boston Children's Hospital during the last 16 years. 67 were admitted originally with a diagnosis of acute nephritis and three with chronic nephritis. 9 of the 67 cases or 13·3 per cent. terminated in chronic nephritis, of which only 2 were severe cases. The average age on admission was $6\frac{1}{2}$ years, the oldest being 12 and the youngest 2 years. At the time of examination the average age was 10, the oldest patient being 19 and the youngest 4. All the 67 patients who had had acute nephritis were living under normal conditions on ordinary diet, and in every case the urine was found to be negative. As regards the 12 chronic cases the average length of time seen after discharge was $2_{\frac{1}{2}}^{\frac{1}{2}}$ years ; 4 were seen 5 years and 2 between 1 and 2 years after discharge. In none of the 7 cases examined was the blood-pressure raised. Of 12 patients examined 8 had a trace of albumin in the urine and 4 none at all. James concludes that the majority of cases of acute nephritis make a complete recovery, but that there is no justification for saying that a child is well on the strength of one or more negative examinations of the urine until the child has lived under ordinary environment and on a regular diet for a considerable period. As regards chronic nephritis he considers that there is no specific guide to prognosis. He believes that many patients with mild chronic nephritis recover, and that many will stand severe infections without acute exacerbations of nephritis, which are most likely to follow upper respiratory affections.

Treatment. Molnar, jun., of the Third Medical Clinic of Buda Pesth University, found that treatment of dropsy in renal and cardiac disease by thyroid tablets, which were first introduced as a diuretic by Heinsheimer in

1895, sometimes had a very good effect. He recommends that in cases where other diuretics fail thyroid tablets should be carefully employed.

Hülse, of the Halle University Medical Clinic, states that calcium chloride was of considerable value in the treatment of the various dropsical conditions which he met with in the course of the war, such as renal dropsy and war oedema. In nephritis it not only acted on the dropsy but often had a surprisingly good effect upon the renal process as such. Owing to the large amount of sodium chloride in the bodies of oedematous patients, large doses of calcium chloride are required, viz. 15–20 gm. a day. Hülse considers that it is owing to neglect of this rule that calcium chloride has not yet been recognized as an efficient drug in the treatment of dropsy. Small doses have no effect. Occasionally the action of calcium chloride is increased by combining it with other neutral salts, especially magnesium salts or urea. The calcium salt acts by exercising an antispasmodic effect on the sympathetic and autonomous nervous system. The fall of blood-pressure following the administration of calcium chloride may be regarded as due to the specific action of the drug on the nerve-endings in the muscular coat of the vessels.

Kretschmer and Helmholtz, of Chicago, treated 11 cases of pyelitis in children aged from 7 months to 10½ years, which had resisted other forms of treatment, by lavage of the renal pelvis with 0·5 per cent. solution of silver nitrate. The amount injected ranged from 1 c.cm. in infants to 5 c.cm. in older children. In 9 of the cases the urine was rendered sterile and free of pus without any complications or unfavourable results.

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J. D. R.
G. W.
C. L.

INFLUENZA

Epidemiology. According to Newman, chief medical officer of the Ministry of Health, during the first three months of 1920 most countries experienced an epidemic wave of a minor kind, but after April they were almost free from the disease. In England and Wales there was a considerable rise in the number of deaths from influenza during the first half of 1920, the culminating point being reached in the week ending March 27. There was then a rapid decline which was only interrupted in the middle of May by an unexplained outbreak in Sheffield. Of the European countries, Austria, Belgium, Holland, Germany, Italy, Poland, and Switzerland suffered more severely during this spring outbreak of 1920 than during the same period of 1919. Of Asiatic countries, Japan experienced a serious outbreak at the end of 1919 which assumed alarming proportions in January 1920, when 300 deaths were reported daily in Tokio. Mild outbreaks were reported in Hong Kong and Shanghai in January and February. In India the influenza deaths reported in Bombay, Calcutta, and Madras numbered only 3,516 during 1920 as compared with 8,954 in 1919. In the Union of South Africa there was a recrudescence of a mild type in July of the epidemic which had occurred during the last six months of 1919, and Durban, Maritzburg, and the Johannesburg districts suffered severely in October and November. A minor epidemic wave occurred in Egypt in the first half of 1920, but only about 4,000 cases in all were recorded. Australia and Tasmania were practically free from a serious form of the disease throughout 1920, but in New Zealand 29,928 cases were notified during the first six months. Relatively mild epidemics occurred in some of the Pacific islands in February 1920. Influenza was epidemic throughout the United States during the first three months of 1920, and the recorded cases in some of the large towns considerably exceeded those recorded during a similar wave in 1919. In Canada influenza was present in epidemic form during February 1920, in the provinces of Montreal and Ontario. An unusually severe epidemic occurred in Mexico in February and March, 671 deaths from the disease being recorded in the city of Mexico alone. Outbreaks also occurred in the Panama Canal zone, Brazil, Bolivia, Cuba, and the Hawaiian Islands during the same period. Jamaica, the Argentine, Uruguay, and Chile, were practically free from the disease during 1920.

Replies to a questionnaire sent by the *Medizinische Klinik* to well-known authorities in various parts of Germany show that the epidemic of influenza which occurred in that country at the end of 1921 was mild, severe cases being exceptional.

Blood. During the 1920 epidemic of influenza among the students of the University of Wisconsin, Bunting made a daily study of the differential leucocyte picture in a small series of cases treated in the University Infirmary. From observations on these cases in conjunction with the work of others he came to the conclusion that uncomplicated influenza had a characteristic blood-picture, which consisted in an early neutrophil leucocytosis followed by a sharp drop to a leucopenia with a marked deficiency in cells of marrow origin and of blood-platelets and with a lymphocytosis of varying degree. There was a gradual return to normal, but cessation of fever and symptoms might be accompanied by a very abnormal blood count.

Symptomatology. Regan, of Brooklyn, gives the following statistics of symptoms obtained from the case histories of 100 patients admitted to the Kingston Avenue Hospital between September 16 and November 10, 1918. The only symptoms that were absolutely constant were headache and cough. The majority of patients had also backache (70 per cent.), sore throat (64 per cent.), and chills (50 per cent.). The remaining symptoms in order of frequency were pain in the limbs (34 per cent.), dizziness or vertigo (29 per cent.), nasal discharge (28 per cent.), vomiting (23 per cent.), perspiration (23 per cent.), discharge from the eyes (20 per cent.), pain in the joints (14 per cent.), diarrhoea (12 per cent.), general soreness of the body (12 per cent.), epistaxis (10 per cent.), pain in the neck (7 per cent.), and pain in the abdomen (4 per cent.).

Stettner, of the Erlangen University Children's Clinic, emphasizes the difficulty in diagnosing *stenosis of the upper respiratory tract* due to influenza from that due to diphtheria. The predilection of diphtheria for the larynx and of influenza for the trachea is not sufficiently constant to justify any conclusions as to differences in the respiratory mechanism. On the other hand, the pathological process in the two diseases is different and is manifested clinically in influenza by catarrh of the bronchi and upper respiratory tract which is absent in pure diphtheria. Therapeutically adrenalin spray is beneficial in influenzal stenosis in association with mustard poultices and cardiac tonics. Intubation is contra-indicated in influenza owing to the tendency of the tissues to necrosis and the presence of the abundant catarrhal secretion which constantly blocks the tube. The indication for tracheotomy depends on the localization of the obstruction to respiration. If the process is confined to the larynx the operation will be of service, but if, as is usually the case, the trachea is mainly involved, tracheotomy only adds a fresh complication.

The occurrence of *chronic lung disease following influenza*, to which reference was made in the last review (vide *Medical Science*, 1921, **4**, 297–8), is discussed by Liebermeister, Treupel and Stoffel, and Bossert and Leichtentritt, in Germany, and Fishberg, in the United States. Liebermeister, of Dürren, has seen 15 cases of this kind in which the clinical appearances closely resembled tuberculosis of the apex, but no tubercle bacilli were found in the sputum. Pirquet's test was negative and no reaction followed injection of 0·1 to 10 mgm. tuberculin. In 7 cases the doses were increased to 200 mgm. old tuberculin and 2,000 mgm. bacillary emulsion without causing any reaction. All but one of the patients recovered, although in some of the cases the atypical signs lasted for several weeks before they finally disappeared. In the fatal case the absence of tubercle bacilli after repeated examinations negatived the diagnosis of tuberculosis in spite of severe haemoptysis, and indicated an influenzal broncho-pneumonia, and the correctness of this diagnosis was confirmed at the autopsy, in which no trace of tuberculosis could be found. Treupel and Stoffel, of Frankfort, who in the course of three years saw 20 examples of this kind among 526 cases of influenza, emphasize the difficulty and occasional impossibility of distinguishing the chronic form of influenza from pulmonary tuberculosis, especially as both diseases may exist concurrently, or one may follow directly on the other. Bossert and Leichtentritt, of the Breslau University Children's Clinic, describe a form of chronic pulmonary disease in children following influenza and characterized by the formation of bronchiectasis and auscultatory sounds in the chest which they compare to the crackling of machine-gun fire. They point out that a correct

diagnosis in such cases will save a tedious and expensive tuberculin cure, sanatorium treatment, and isolation from the family.

Tristan devotes his Paris thesis to a consideration of the *gastro-intestinal forms* of influenza, of which he describes the following four varieties: (1) pure gastric form; (2) pure intestinal form; (3) a mixed gastro-intestinal form; (4) a form characterized by gastro-intestinal haemorrhages. The first two forms are the rarest. Tristan points out that the gastro-intestinal forms of influenza must not be confused with the gastro-intestinal symptoms which develop in the course of influenza, and are due to well-known micro-organisms such as typhoid, paratyphoid, or dysentery bacilli. He quotes instances of old gastro-intestinal affections, such as gastric ulcer or amoebic dysentery, being roused into fresh activity by an attack of influenza.

Alexander, of Berlin, who in the 1918 epidemic had met with intestinal disturbances in 20 per cent. of about 800 cases of influenza, observed similar symptoms in the epidemic at the beginning of 1921. The patients suffered from diarrhoea with 12–20 stools in the twenty-four hours, and severe tenesmus, high fever, vomiting, and prostration. Bronchial and pulmonary complications were rare, but nervous symptoms, such as severe neuralgia and pain in the back, were frequent. The duration of the disease in such cases ranged from three days to several weeks. Treatment consisted in vigorous purgation. Commenting on Alexander's paper, Schwalbe records a case of abortive intestinal influenza which lasted only two days, though the patient required 10 days to recover, five of which were spent in bed.

Nervous complications. Klein, of Prague, records six cases of polyneuritis which developed on the average three weeks after the acute symptoms of influenza had subsided. All the cases were in women, and three were members of the same family (grandmother, mother, and daughter), The symptoms consisted of spontaneous pain, marked tenderness of the muscles and nerve-trunks, disturbance of the reflexes, and, in severe cases, of flaccid paralysis of symmetrical distribution with partial reaction of degeneration. Sensory disturbances occurred in the form of a combination of hyperalgesia of the skin and hyperaesthesia to touch and temperature, with disturbance of stereognosis. Three cases showed a combination of polyneuritis with symptoms of encephalitis, and in one of these cases there was also possibly a spinal cord lesion in the form of poliomyelitis. Treatment consisted at first in warm applications, diaphoresis and salicyl medication, and later in electrical treatment. All the cases responded very well to treatment except one, in whom the symptoms were probably due to poliomyelitis.

Curschmann, of the Rostock University Medical Policlinic, describes three examples of spasm of the glottis and deglutition following influenza, he himself being the victim in one case. The features noted in each case were the occurrence of attacks of spasm of the glottis, principally at night, without any special psychical cause, accompanied by a violent swallowing of air, in the absence of all signs of bronchial asthma, tetany, tabes, polyneuritis, encephalitis, or whooping-cough. Curschmann attributes these attacks to a transient ascending irritation of the sensory fibres of the superior laryngeal nerve, caused by influenzal laryngo-tracheitis.

In March 1921, Reilly, of New York, observed a group of patients presenting as a characteristic symptom an unusual localization of pain in association with other symptoms of influenza. The pain, which might be

paroxysmal or continuous, was on the right side, usually on a level with the insertion of the diaphragm. In many instances the pain shifted within 36 hours to the left side at the same level, but was less severe, sometimes entirely disappearing from the first side affected. The paroxysms were sometimes accompanied by nausea. Change of location of the pain on the second day to the opposite side made it easy to rule out cholecystitis, and diaphragmatic pleurisy was excluded by the evanescent character of the symptoms, which was explained by the presence of an exudate between the nerve-bundles that was quickly exuded and as quickly absorbed.

Semenow, of Stara-Zagora, Bulgaria, records a unique case of acute myelitis of influenzal origin in a woman, aged 36, in whom the lesions were confined to the sacral region. Recovery followed laminectomy, at which about 100 c.cm. of clear fluid were evacuated.

According to Menninger, whose previous papers on influenza and the nervous system have been abstracted (vide *Medical Science*, 1919, **1**, 253; 1921, **4**, 300), the effect of influenza on epilepsy is not uniform. A beneficial influence is occasionally observed; seizures are usually absent during the febrile state, and sometimes occur with decreased frequency after the acute infection. Deleterious influence, however, is more frequent; seizures may be more frequent and severe, epileptic attacks which have long been latent may be incited to renewed activity, and complicating psychoses may be produced. Epileptiform syndromes which resemble typical idiopathic epilepsy, except that recovery usually occurs shortly, are occasionally evoked by influenza, being possibly the manifestations of multiple miliary (encephalitic) haemorrhages. Menninger found, however, that the majority of epileptic patients who had influenza did not show a change in their disease. The effect of epilepsy on influenza was observed to be a lowered resistance, and hence increased incidence and mortality rates as compared with the normal.

Hannah alludes to the cases of post-influenzal epilepsy recently described by Clark (vide *Medical Science*, 1920, **2**, 423), and records a case in a man aged 22, with an unimportant family and personal history, in whom the first seizure occurred simultaneously with the onset of influenza. The attacks at first numbered from two to three weekly and gradually increased to three to twelve daily.

Vormann describes his own attack of post-influenzal *myositis*, in which the right gastrocnemius and soleus were involved. Only two other cases of this complication have been recorded, namely, by Hildebrandt and Burger. [Vorpahl has also described a case, vide *Medical Science*, 1920, **2**, 117–18.—J. D. R.] The case was further of interest in that the diagnosis was confirmed by the serum agglutination test.

Surgical complications. Roello, of the Florence Institute of Surgical Pathology, describes two cases in children, aged 13 months and 3 years respectively, of *suppurative arthritis* in influenza, the only examples of this complication which occurred during the mild epidemic in the early months of 1920, none having been seen in the severe epidemic of 1918–19. In one case the right shoulder-joint and in the other the left elbow and right hip were involved. Complete recovery took place in the first case, in which Gram-negative diplococci were found, while in the second case, in which a diplostreptococcus was isolated, 2 cm. shortening of the lower limb resulted.

Fieber, of Vienna, reports a fatal case of so-called spontaneous rupture of the spleen, associated with influenza and purulent appendicitis, in a man aged 29, the cause of death being internal haemorrhage. The rupture of the

organ was attributed to sudden increase of intra-abdominal pressure, while the subsequent vomiting increased the haemorrhage.

A case of osteomyelitis of the patella following typical influenzal broncho-pneumonia is reported by Duguet in a soldier. Recovery followed removal of the patella.

According to Laurens and Gand, the frequency of **aural complications** in influenza is 12 per cent. Occasionally infection of the ear may be the only manifestation of influenza. Influenzal otitis may assume all the forms of otitis media. In addition to those which clear up rapidly without leaving any trace, are prolonged forms with dangerous intracranial complications or chronic lesions of the tympanum. In most cases, however, the otitis has a sudden onset, suppuration is profuse, and recovery rapid. The complication is more frequent in young subjects, especially children with adenoids. The internal ear is rarely affected. Either concurrently with otitis media or independently, influenza may give rise to a special type of infection in the external auditory meatus, manifested by the development of phlyctenules with serous or haemorrhagic contents. The symptoms are severe otalgia accompanied by tinnitus and slight impairment of hearing. The affection lasts only two to four days, the pain ceases suddenly, and the phlyctenules rupture and dry up.

De Kerangal records three cases of unilateral *frontal sinusitis* following influenza successfully treated by operation.

Denyer, of Hull, records the case of a girl aged 17 who, in convalescence from influenza, developed papillitis characterized by *blindness* of rapid onset and frontal and temporal pain. The sight was gradually recovered in the course of three or four weeks. There was no evidence of cerebral tumour or abscess, and the Wassermann reaction in the cerebrospinal fluid was negative.

A case of supposed blindness after influenza was shown by Aitken to be merely a blurring of vision due to a low degree of hypermetropia exaggerated by weakness of the ciliary muscle resulting from influenza.

Influenza and tuberculosis. Dealing with the relation of influenza and influenzal pneumonia to pulmonary tuberculosis, Dickinson, tuberculosis officer for Newcastle-on-Tyne, publishes figures suggesting that the importance of influenza as an activator of pulmonary tuberculosis has been much overrated. In 1919 there were notified 297 cases of lobar pneumonia, 269 of influenzal pneumonia, and 38 of other forms of pneumonia. Many of these cases terminated fatally, and some could not be traced, but investigations of the remainder showed that though much ill health had followed these diseases, notably in the case of influenzal pneumonia, only 6 had subsequently been notified as suffering from pulmonary tuberculosis. In contrast to these findings there was the significant fact that 42 of the 274 (15·3 per cent.) new sputum-positive cases registered between June 1, 1918, and June 30, 1920, gave a history of influenza as the starting-point of the illness. Dickinson suggests, as an explanation for the discrepancy of these two series of figures, that many cases of tubercle of the lung begin very acutely with symptoms so closely resembling those of influenza that this disease is diagnosed by the patient.

In a discussion of the aetiological importance of the influenza epidemic of 1918–19 on some chronic forms of pulmonary tuberculosis, Crouzon and Marceron state that among the cases of severe pulmonary tuberculosis examined by them between June 1, 1920, and January 1, 1921, 7 per cent.

gave a history of having had influenza in 1918 or 1919, in 6 per cent. this attack started or aggravated their lung condition, and in 4 per cent. the attack of influenza had no effect upon their tuberculosis. In no instance was the attack of influenza followed by a lull in the tuberculous process.

Influenza and malaria. An outbreak of influenza which occurred among 150 cases of malaria at the County of London War Hospital, Epsom, in September 1918 is described by King. 71 or 47·3 per cent. contracted influenza, and out of 54 of these cases in which the type of malarial parasite was identified 38 or 70·4 per cent. were of the malignant tertian type, 15 or 27·7 per cent. were of the benign tertian type, and in 1 or 1·8 per cent. of the malignant tertian and benign tertian combined. The mortality was 11·2 per cent., which was a remarkably low figure for cases of concurrent malaria and influenza. In Leitner's cases the mortality was 80 per cent., and in Matko's cases 78 per cent. (vide *Medical Supplement*, 1912, **2**, 166).

Influenza in the new-born. Briz, of Madrid, records a fatal case of influenza in a new-born infant which had a severe cough and attacks of laryngospasm a few hours after birth. The mother, father, and three other children in the family were suffering from influenza at the same time. Death took place on the twelfth day of life. A remarkable feature in the case was that the disease was not accompanied by any rise of temperature. Briz thinks that the infection was acquired *in utero*, as the child had a cough a few hours after birth, and breast-fed children are immune to the majority of infectious diseases.

Influenza in nurses. King has made a study of the influenza epidemic of 1918–19 amongst the nursing staff of the County of London War Hospital Epsom. Of 329 nurses 84 contracted influenza and 2 died. The types of severity of the cases were as follows: fatal 2, severe 5, moderate 17, slight 61 (including 1 readmission). The duration of contact before infection varied from 1 day to 6 weeks, and was slightly longer among the nurses who worked in wards with severe types of influenza complicated by pneumonia than among those attending mild and uncomplicated cases. On the other hand, all the severe and fatal cases but one had been on duty in wards containing severe cases complicated by pneumonia.

Immunity. The following figures published by Glaessner, of Vienna, indicate that influenza confers a certain immunity. Of 618 cases of influenza only 75 or 12 per cent. had had a previous attack, and among these only 6 ended fatally—a mortality of 8 per cent. as compared with 78 deaths or a mortality of 12·6 per cent. among the 618 cases (cf. *Medical Science*, 1921, **4**, 303–4).

Treatment. Willmore and Gardner-Medwin recommend a treatment the object of which is twofold: (1) to stimulate leucopoiesis directly by hypodermic or intramuscular injection of sodium nucleinate; and (2) to neutralize the poison already circulating in the tissues by large doses of alkalis (sodium bicarbonate 1 drachm four-hourly), and by giving as much glucose in the food as the patients would take. In the worst cases glucose was also given by rectum. The writers record 12 illustrative cases with pulmonary complications, all so seriously ill that a fatal issue was reasonably anticipated, but in whom a nucleinate injection produced a considerable rise in the leucocyte count followed within 48 hours by a true critical fall of temperature.

Glaessner states that intravenous injection of a 10 per cent. solution of glucose in doses of 200–300 c.cm. appeared to save life in several cases. No

ill effects of any kind were observed in more than a hundred injections. Mustard packs and mustard baths which were followed by a powerful leucocytosis were also of value. In a number of cases the attack could be cut short by intravenous injection of *B. coli* vaccine.

Demmer, of Frankfort, reports 10 cases showing that injections of camphor oil in the treatment of influenza may not be absorbed even after several weeks, but that infiltrative phlegmonous processes may develop at the site of infection a long time after apparent subsidence of the infection. He therefore deprecates the use of camphor-oil injections in the treatment of influenza, and recommends the use of some substitute, such as camphor-water intravenously or camphor internally, which is equally efficacious without possessing any deleterious action.

Subcutaneous injections of oxygen are advocated in all forms of influenza by Bayeux, who recommends that they should be given at an early stage of the disease and continued as long as the fever and symptoms of respiratory insufficiency persist.

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J. D. R.

C. L.

ABSTRACTS

SURGERY

Strauss. Torsion of the gall-bladder. *Beitr. z. klin. Chir.*, 1921, **122**, 322–3.

Torsion of the gall-bladder on the cystic duct as pedicle is very rare. Krattel (*Deutsche Ztschr. f. Chir.* vol. 152, f. 1 and 2) recently collected six cases. Strauss adds a new one in a very fat woman of 40 years, who had been seized with sudden violent abdominal pain accompanied by slight fever. With difficulty a lump was felt in the right flank and another towards the pyloric region. There was no jaundice; pulse-rate was 108. At operation the gall-bladder was found very distended and surrounded with recent and old adhesions; the omental adhesions were tied and divided and the gall-bladder removed. The gall-bladder was found to be reniform, with the cystic duct arising, not from the inner pole, but from the junction of inner and middle thirds of the surface that presented towards the middle of the abdominal wall; hence the sensation of two swellings felt before operation. The gall-bladder showed torsion through 180 degrees on the axis of the cystic duct. The reniform shape is believed to be an important predisposing cause of the torsion (Krattel). C. C. C.

Lett, Hugh. Torsion of the gall-bladder. *Brit. J. Surg.*, 1922, **9**, 464.

In this paper Lett republishes his case of torsion of the gall-bladder which had been previously published in the *Lancet* of 1909, but which had largely been overlooked by subsequent writers. The patient was a woman of 72 with a history of sudden onset of severe pain in the right hypochondrium 3 days previously. She had vomited 4 or 5 times and the bowels had not acted since the beginning of the attack. No similar pain before; no history of gall-stones. On examination her temperature was 101°, and pulse-rate 100; there was great tenderness and rigidity in the right upper abdomen and a rounded tumour in the region of the gall-bladder. The abdomen was distended. Operation disclosed an enlarged gall-bladder and numerous recent adhesions to omentum and to hepatic flexure of the colon. The gall-bladder was black and the size of a large pear. It was actually rotated on the cystic duct; the twist was easily undone and consisted of four half-turns from left to right (counter clockwise). The gall-bladder and part of the cystic duct were excised. The patient collapsed and died 12 hours after operation. C. C. C.

Irwin, S. T. Torsion of the gall-bladder. *Brit. J. Surg.*, 1921, **9**, 310.

Irwin also records a fresh case of this rare condition. The patient was a woman of 34, married, with one child six months old. Twenty-six hours

before admission to hospital she had been suddenly seized with acute and very severe epigastric pain. Vomiting was frequent but did not relieve the pain; it had ceased before she came into hospital. There was no jaundice, nor distension of the abdomen, nor visible peristalsis; the abdomen moved with respiration; temperature was 99°, and pulse 90. There was great tenderness over the gall-bladder. She had had attacks of biliousness since girlhood, and immediately after her confinement six months previously she had had a similar, though less severe, pain. Operation revealed a gangrenous gall-bladder, tense and black in colour; it was found to have been twisted clockwise through 360 degrees. The twist was in the proximal part of the gall-bladder itself, but did not involve the spiral valve. The blood-vessels were completely strangulated and the contents were blood with a trace of bile.

Irwin gives a short bibliography of 7 previous cases in which the main points were: (1) advanced age of the patient; (2) the absence of gall-stones, which were found in only one case; (3) the difficulty of accurate diagnosis before operation, and (4) the success of laparotomy. C. C. C.

Magoun, J. A. H., and Renshaw, K. Malignant neoplasia in the gall-bladder. *Ann. Surg.*, 1921, **74**, 700.

A brief review of the literature is given, in which it is shown that the frequency of carcinoma of the gall-bladder with gall-stones has varied from about 1·5 per cent. to 10 per cent.

An investigation of the pathology has usually revealed that the growth is nearly always carcinomatous and generally of the columnar type. Owing to a metaplastic change, a squamous carcinoma may be found. Primary sarcoma is exceedingly rare. The growth is most commonly found in the fundus, but it may arise in the neck or be diffuse in form. It is generally admitted that the malignancy is dependent upon the presence of calculi, and published statistics show that stones have been found in from 70 to 95 per cent. of the cases. The majority of observers have agreed that the carcinoma is secondary to the calculi, although some have held that it is the presence of the growth which has given rise to the formation of stones.

Some 70 to 80 per cent. of the reported cases have been females, but Smithies found 16 males and 7 females. The average age is between 50 and 60 years, but a case has been reported in a boy aged 4.

As a general rule the results of operation have been poor. The authors state that from January 1907 to January 1921 there were 7,878 operations for gall-stones at the Mayo Clinic, and within this period there were 84 cases of primary malignancy, 83 of which were carcinomatous. As a general rule the carcinomas were of the adenomatous type and formed papillary or ulcerative growths, but in 23 of the cases there was a diffuse form with general thickening of the walls of the bladder. A cholecystectomy was performed in 38 cases and in 37 of these gall-stones were present. Of the 46 explorations, calculi were present in 33. Sixty-eight of the patients were females and sixteen males.

As a general rule the symptomatology dates back for a prolonged period, the average being 10 to 13 years, but in one there had only been symptoms for a month. The symptoms were those of calculi, but in 38 there was the radiation and pain to the back which is so often found with carcinoma. Jaundice was present in 40, and 47 vomited. Of 33 patients in whom

a test meal had been taken there was the characteristic sub-acidity of calculi. The cases can be divided into three groups: (1) Those in which there was a sudden change after symptoms of gall-stone colic had been present for years. The patient begins to lose weight and strength, and the pain becomes continuous. (2) Those similar to group one, but with the exception that instead of gall-stone colic there had only been previous symptoms of gall-bladder dyspepsia. (3) Cases in which there were no symptoms up to a year before operation, when there was a sudden development of the symptoms of malignancy.

Stress is laid upon the difficulty of diagnosing carcinoma in this position sufficiently early to obtain good operative results. The symptoms are usually those of calculi, and there is but little evidence of the onset of malignancy until the late stages. Of the 84 cases a cholecystectomy was only possible in 38, and in 6 of these it was necessary to remove a portion of the liver. Of the whole, exploration showed that the growth had extended either to the liver or some other surrounding viscus in 77. The operative mortality was not very high, there being eight deaths within two weeks of operation. Seven patients were alive six years after operation, a percentage of 8·3 cures. A. J. W.

Stewart, W. D., and **Barber, W. H. Acute perforated ulcer of the stomach or duodenum.** *Ann. Surg.*, 1922, **75**, 349–55.

The authors contend that, in the closure of perforating juxtapyloric ulcer by simple inversion, the anterior surfaces of stomach and duodenum can be sutured in apposition to one another without fear of pyloric stenosis. In support of this they quote 5 experiments on dogs, in which a hole was burned in the ventral side of the pylorus and closed by inversion with two purse-string sutures, followed by plication of the duodenum across the anterior face of the pyloric end of the stomach. At the end of each 24-hour interval after operation one dog was given an opaque meal and X-rayed up to 5 hours, after which the stomach was removed for examination.

Up to three days after operation there was a 5-hour residue, and the pylorus did not allow passage of the tip of the little finger. In the four- and five-day animals the stomach was empty in five hours, and the tip of the little finger could be passed through the pylorus.

They conclude that pyloric obstruction need not be feared after simple inversion of a perforating ulcer in man, and consider that gastroenterostomy, when performed on account of fear of stenosis, is an unnecessary addition to the operation. The indication for gastroenterostomy introduced by the possibility of contraction in the base of a chronic ulcer is not considered.
E. K. M.

Johnson, Raymond. Carcinoma of the jejunum and ileum. *Brit. J. Surg.*, 1922, **9**, 422–33.

Raymond Johnson records three cases and reviews the subject. He excludes duodenal and ileo-caecal growths.

Carcinoma of jejunum and ileum, distinctly uncommon anywhere, is commoner near the extremities than elsewhere, but is much less rare in the lower part of the ileum than in the upper part of the jejunum. As emphasizing the rarity of the disease, the author quotes statistics: among 41,838

autopsies at the Vienna General Hospital, 343 were intestinal cancers, of which 10 were in the ileum and none in the jejunum; and among 584 intestinal carcinomas, collected by Hintz, 18 (3·08 per cent.) were in the small intestine, excluding the duodenum. The infrequency of carcinoma in jejunum and ileum may perhaps be explained by the fluidity of the contents, the absence of sharp bends, and the freedom from stasis so often seen in the large gut.

Of Raymond Johnson's cases two were jejunal and one ileal. The first case was in a woman, aged 46; projecting into the lumen of the jejunum there was a small narrow-based carcinoma, which had become involved in an intussusception and was only obvious after this had been reduced. Resection was done and the patient was alive and well six years afterwards. The second patient was a man, aged 32, with a two weeks' history of abdominal fullness, constipation, and vomiting, and a 'rolling sensation' about half an hour after food. A tight annular nodular constriction was found in the jejunum, below distended gut; resection was done, but the patient died 9½ months later with hepatic and other abdominal recurrences. The third patient was a woman, aged 32, with a six months' history of attacks of abdominal pain soon after food, with occasional vomiting, which relieved the pain; distressing flatulence and constipation were present. There was a very hard growth, feeling like a Murphy's button, about six inches above the ileo-caecal valve. Obstruction was so great that the gut above was drained for 12 days; then the growth, artificial anus, and 13 inches of ileum with its mesentery were removed. Recurrence took place. The growth was a tight annular stricture of the nature of a columnar-celled carcinoma; a mesenteric gland was involved.

In all three cases marked visible peristalsis was a prominent feature. In the two jejunal cases the distension and the visible peristalsis, from right to left, were limited to a single coil lying transversely in the umbilical zone; but the ileal case presented a different picture, for here there was considerable general distension and there was a marked 'ladder pattern' of peristalsis visible in 4 or 5 transverse coils.

A point of interest in the ileal case was the shifting dullness, although at operation there was no free fluid in the peritoneal cavity; at operation it was seen that this was due to the shifting of intestinal coils loaded with fluid contents.

The almost constant symptoms, before the onset of complete obstruction, are abdominal pain, vomiting, increasing constipation, and often rapid emaciation. The pain is usually paroxysmal and coincident with peristaltic waves, if those be visible. Vomiting is very constant, and, like the pain, may or may not be associated with meals; it is often misleading to assume that the higher the growth the closer the relation to meals. The pain is frequently accompanied with much gurgling. Constipation is increasingly obstinate; it does not alternate with diarrhoea, as is so commonly the case in carcinoma of the colon. Blood in the stools is exceptional. Detection of the abdominal tumour before operation is rare.

The duration of symptoms before operation varies between two weeks and a year.

The treatment is resection. If obstruction be marked, a preliminary artificial anus should be made above the growth; this cannot be left to drain very long, partly because of the rapid emaciation associated with an opening so high in the gut and partly because of damage to the skin by the

irritating contents of the small intestine; therefore, after a short interval, artificial anus and growth should be resected together.

Four varieties of the primary growth may be recognized, viz.: (1) the stenosing, ring-stricture form; (2) the polypoid form, projecting into the lumen; (3) the ulcerative form, and (4) colloid carcinoma. Occasionally the growths, although definitely malignant and causing metastases, are multiple, one of them being the parent of the others. Intussusception or acute perforative peritonitis may be caused, the former more frequently than the latter. Fistulous communication may occur with other loops of gut. Metastases are frequent, especially in mesenteric glands, peritoneum, and liver; they have been seen in lungs, bones, and in spinal dura.

Histologically, carcinoma of the small gut is usually columnar-celled, but sometimes spheroidal- or polygonal-celled. The author's two ring-stricture cases were columnar-celled; the polypoid one was polygonal-celled. The spheroidal-celled form is probably the more malignant.

In conclusion, Raymond Johnson refers to the multiple 'carcinoid' tumours occasionally found *post mortem* in the small intestine, which, although microscopically resembling carcinoma, show little or no evidence of malignancy. These have been described by Bunting as 'multiple primary carcinomata of the ileum', and by Krompecher as 'basal-celled tumours of cylindrical-celled mucous membranes'. Consisting of small spheroidal cells, these multiple tumours are supposed to take origin in the basal cells that lie between the cylindrical cells of the crypts of Lieberkuhn in intestine and appendix; they are allied to the basal-celled tumours of the skin, and, like them, are of low malignancy. C. C. C.

Grégoire, R. Technique de la duodéno-jéjunostomie. [**Technique of duodeno-jejunostomy.**] *J. de Chir.*, 1922, **19**, 449–55.

Grégoire gives a full account of the anatomy of the operative field and points out that this is strictly determined by the size of the angle between the transverse mesocolon and the root of the mesentery, an angle which varies within wide limits. In the usual circumstances under which the operation is performed the dilatation of the third part of the duodenum opens up this angle sufficiently to enable an anastomosis by suture to be carried out on the ordinary lines. When the operative field is unduly restricted by a low transverse mesocolon or an unusually horizontal mesentery, he recommends a Y-anastomosis. This modification he has not, himself, had an opportunity of practising, but it has been done by Duval. The article is clearly illustrated. E. K. M.

Backman, W. Ueber die Rolle des Geschlechts in der Ätiologie der Appendizitis. [**The part played by sex in the aetiology of appendicitis.**] *Acta Med. Scand.*, 1922, **56**, 478–84.

After surveying the literature of the sex incidence of appendicitis, Backman analyses the 933 cases of appendicitis operated on in hospital in the period 1909–15. In 274 cases the appendicitis was destructive, in 659 it was catarrhal. In the destructive class the numbers were approximately equal, males being represented by 51·5 per cent., females by 48·5 per cent. But in the catarrhal class the sex difference was striking; males were represented only by 29·4 per cent., females by 70·6 per cent. It might be suggested that the preponderance of females in this class was due to mis-

taken diagnoses in nervous women, but, though this may have been the case in a few instances, Backman does not accept this explanation as the main reason for the comparative frequency of catarrhal appendicitis in women. He has re-classified his cases of catarrhal appendicitis according as definite macroscopic changes were or were not found in the appendix at the time of operation. In the second group there were only 7 males to 58 females, whereas in the first group there were 187 males to 407 females. He associates women's comparative liability to develop catarrhal appendicitis with their sedentary habits, and in this connexion he notes that in the catarrhal class of appendicitis 50 per cent. of the females, but only 24 per cent. of the males, suffered from chronic constipation. On the assumption (and Backman admits that this assumption is not invariably correct) that destructive appendicitis passes through a preliminary catarrhal stage, it follows that 141 out of 335 cases of catarrhal appendicitis in males terminated in destructive appendicitis. This gives a percentage of 42·1. On the other hand, only 133 out of 598 cases of catarrhal appendicitis in females terminated in destructive appendicitis. This gives a percentage of only 22·2. In other words, catarrhal appendicitis in the male develops into destructive appendicitis in a much greater proportion of cases than in the female. The explanation is to be found in the blood-supply to the appendix, which comes from one source in the male, two sources in the female.

C. L.

Carnot, P., et **Libert, E.** Un cas de cancer de l'ampoule de Vater diagnostiqué par l'examen du suc duodénal. [**A case of cancer of the ampulla of Vater diagnosed by examination of the duodenal fluid.**] *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1921, **45**, 836.

The authors lay stress on the value of the examination of the duodenal contents withdrawn with Einhorn's tube; in a case of obstructive jaundice, they regard the absence of bile, together with the presence of pancreatic secretion and of blood in the duodenal contents, as indicative of carcinoma near the ampulla. With improved technique they hope to detect fragments of growth.

C. C. C.

Klein, E. Embolism and thrombosis of the superior mesenteric artery. *Surg. Gynec. & Obst.*, 1921, **33**, 385–405.

In this full paper Klein discusses the question generally. He believes that although the condition is a rare one it is less so than is generally thought, when account is taken of the cases, probably undiagnosed, that recover spontaneously. In discussing the aetiology, he points out that intestinal infarct may be caused by obstruction either of artery or of vein. The artery may be obstructed by an embolism coming from the left heart or the aorta; arterial thrombosis is generally associated with general arteriosclerosis. In the vein, on the other hand, thrombosis is the only mechanism; in the majority of cases it follows acute appendicitis or an infection of the female pelvic organs. Embolism causes sudden obstruction; thrombosis, whether arterial or venous, is more slowly progressive.

Experimentally, Klein caused circulatory obstruction in the mesenteric vessels of animals by various methods, such as arterial ligature, venous ligature, artificial embolism, detachment of portions of mesentery, &c.

Ligature of the mesenteric artery in a dog immediately produced violent

intestinal tetanic contractions associated with anaemia lasting 2 or 3 hours; this was followed by relaxation associated with congestion and infarct-formation.

Ligature of a branch of the mesenteric artery caused no trouble.

Ligature of the mesenteric vein always led to infarction; injection of paraffin produced similar results.

Neiderstein has shown that a detachment of the mesentery 3 cm. long caused superficial necrosis of the mucous membrane; one 5 cm. long produced necrosis of mucous membrane, infarcts of intestinal wall, and localized ulceration. To cause death, detachment of more than 5 cm. is necessary. These experiments demonstrate the efficiency of the submucous anastomosis. The interesting point is the existence of circulatory lesions, not necessarily fatal. Similar conditions can exist in man, probably more frequently than is realized, because the mesenteric vessels are seldom completely dissected out in autopsies. Where sought, such lesions are sometimes found; thus Nazari found 7 cases of arterial obstruction due to arteriosclerosis in 1,700 necropsies, yet only one showed resultant infarct; Schley, in 1,600 post-mortem examinations, found 4 thromboses that had given more or less symptoms during life, and 4 in which very few intestinal symptoms had attracted attention to the mesenteric vessels. It is established that a progressive thrombotic obstruction may be unaccompanied by any intestinal lesion because the collateral circulation has had time to establish itself.

Other factors than the obstruction itself must be taken into account, especially cardiac disease, in order to explain fatality from infarction when the artery is incompletely obliterated. Sometimes incomplete thrombosis can cause death not by infarction but by intestinal obstruction; the circulation remaining, in such case, suffices to maintain the life of the intestine (without infarction) but not to maintain its motor function. As for obstruction of the superior mesenteric vein in man, it has a progressive rather than a sudden onset; but in spite of this it may be followed by infarction. Reich has shown that, in these cases, the process has spread into the branches of the vein, even right up to the intestine.

Symptomatology. Pain, constipation, vomiting, and blood in the stools are present in combinations and degrees varying with the intensity of the process, from the rapidly fatal form to that in which recovery may occur; in the latter cases the intestinal circulation may be completely re-established; or it may recover for a time and be competent until a later increase of visceral sclerosis or of myocardial disease throws too heavy a strain upon it.

The only **treatment** of mesenteric infarction is resection of the affected segment of gut. Twenty-four successful operations of this kind since 1895 are recorded. For the milder non-fatal cases the general treatment for arteriosclerosis is adopted and intestinal work is reduced by giving frequent small and easily digested meals. C. C. C.

Fasano, M. Arteriotomia della femorale per trombosi con incipiente gangrena dell' estremità. Guarigione. [**Arteriotomy of the femoral artery for thrombosis with incipient gangrene. Cure.**] *Arch. ital. di chir.*, 1922, **5**, 207.

The patient, a man of 68, was operated upon in October 1920. He had had lancinating pains in the left foot for about a month, and for two or three days the fourth and fifth toes had been discoloured. He was a pallid,

feeble old man; the heart, though normal in percussion area, was unsound; the pulse was hard, slow, irregular, and intermittent. The arteries were tortuous and hard. Pulsation could be felt in the left femoral artery only for 3 cm. below the crural arch. Below this could be traced a hard nodular cord in the course of the artery. The two toes were gangrenous. The arterial wall was incised for 3 cm., beginning about 1 cm. below the point to which pulsation extended. A compact, grey, adherent thrombus was revealed. The hand was passed down along the vessel as far as the opening in the adductors and the whole clot squeezed upwards out of the wound in the vessel-wall, emerging in numerous fragments. A covered clamp was put on the lower end as soon as blood flowed. A similar manœuvre cleared the upper end and was followed by a forcible gush of blood, quickly controlled by forceps. The wound was then sutured with silk and the forceps removed. Pulsation immediately returned throughout the palpable extent of the vessel.

For twenty-four hours the dorsalis pedis was palpable; the pains gradually diminished and ultimately disappeared; the fourth and fifth digits separated spontaneously and their stumps cicatrised soundly. Ten months later the gait was normal, there were no pains, and though the arteries at the ankle were not palpable, the femoral pulse extended for nearly 7 cm. below Poupart's ligament.

It is obvious that this is a very exceptional case, for the thrombus certainly reformed as usual, but as it did not extend so far as the opening of the profunda, collateral circulation was re-established. No other cause than senility is advanced for the initial thrombosis. E. R. C.

Kowitz, H. L. Luftembolie oder Pleuraschock? [**Air embolism or pleural shock?**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 374–83.

Kowitz reviews the observations of Brauer, Wever, and others who have shown that all the sudden deaths associated with puncture of the chest may be traced to air embolism, and he notes that the clinical, experimental, and post-mortem evidence in support of this view is still inadequately appreciated by the majority of specialists in the surgery of the chest. There seem yet to be writers who cling to the notion that fatalities can be due to pleural reflex or shock. Kowitz records in detail four cases of air or gas embolism observed during the past eighteen months in Hamburg. The first two patients recovered; the other two died of the effects of the embolism. The recoveries were probably due to the injured blood-vessels being situated in healthy pulmonary tissue in which they could retract and close; in the two fatal cases the injured blood-vessels proved to be situated in diseased structures which kept the wounded blood-vessels gaping. Kowitz also reviews the literature of the controversy, air embolism *versus* pleural reflex. C. L.

Douarre, M. Deux 'incidents' de pneumo-peritoneum. [**Two 'incidents' in pneumo-peritoneum.**] *J. de radiol. et d'électrol.*, 1921, **5**, 368.

After injection of two litres the patient was screened in the upright position. There was immediate pain in the neck and subcutaneous emphysema appeared above both clavicles. Recovery after two days' rest. Presumably the gas travelled through a rent in the diaphragmatic peritoneum,

up the posterior mediastinum, and out into the neck. A similar case was recorded by Lorey (*Medical Science*, 1922, **6**, 309). The second case illustrates the slow rate of absorption of atmospheric air from the peritoneal cavity. Three weeks after injection of two litres there was still a gap of 3 cm. between diaphragm and liver. This source of 'incidents' is, however, a well-recognized one. E. K. M.

Hanssen, T. S. Extremitetsfrakturer. [**Fractures of the limbs.**] *Medicinsk Revue*, 1922, **39**, 133–71.

The chief feature of this long paper is the attempt made by statistical comparison to show the extent to which Lane's osteosynthesis with plates has improved the ultimate results of the treatment of fractures. In 1912 Manthey published the results of treatment of fractures of the limbs at the Surgical Department A of the Riks-hospital in Christiania in the period 1908–11. He found that among 273 fractures the results were good in 73 per cent. and bad in 26 per cent. Hanssen has investigated the results obtained in the same hospital between Jan. 1, 1914, and July 1, 1920, in which period 354 fractures were treated. Information as to the ultimate results was obtained by question forms addressed to the patients a year after discharge or by personal examination. Only in 32 cases could no information be obtained.

The first, and not unexpected, observation was that among insured persons only 46 per cent. were not in receipt of compensation, whereas 75 per cent. of the uninsured reported that they were as well as ever. Hanssen classifies his results according as they were good, bad, or indifferent, the 'indifferent' class being represented by cases with shortening of more than 2 cm. or slight functional disturbances. The 'bad' class included those cases in which there was marked shortening or invalidism. The cases were also classified according as the fractures were recent or of old standing. After discussing each class of fracture by itself, Hanssen notes that among recent fractures the results were considerably worse for the lower than for the upper limbs, this difference being determined chiefly, but not wholly, by fractures of the neck of the femur. The reverse observation was made in the case of fractures of old standing, the results being far worse in the case of the upper limbs. This was due chiefly to the bad results associated with pseudarthrosis antebrachii. The results of *operative* treatment of fractures of old standing were better for the lower than for the upper limbs; in the latter class they were very disappointing, old-standing fractures of the hand and forearm often being incapable of complete operative repair. In the case of recent fractures, the *operative* results were somewhat better for the lower than for the upper limbs, the difference being determined by the success of suturing fractures of the patella. The difference in the results of operative treatment in recent and old fractures was great, stressing the unwisdom of adopting operative treatment as the ultimum refugium.

Pseudarthroses were present in 24 of the 48 fractures of old standing, and among the recent fractures there were 14 cases in which pseudarthroses developed during prolonged treatment in hospital. The total of 38 pseudarthroses could be classed in 3 approximately equal lots, with results good, bad, and indifferent. Of 9 not operated on, there were 3 in each of these categories. Of 27 operated on (plating), 8 showed good, 10 indifferent, and 9 bad results. The fate of the remaining 2 patients was unknown.

To compare his results with Manthey's, Hanssen adds his 'indifferent' to his 'good' results, obtaining a total of 226 favourable results in the treatment of recent fractures. He thus gets 83 per cent. favourable results as compared with Manthey's 73 per cent. In other words, new methods of treatment, of which Lane's is the most important, have added approximately 10 per cent. to the class of favourable results. Lane's operation was carried out in just over 10 per cent. of all the cases of recent fracture. The influence of age on the results was partly obscured by the fact that many of the worst fractures occur between the ages of 20 and 30. But on the whole the proportion of good results dwindles steadily with age, and that common fracture of old age—fracture of the neck of the femur—is apt to place in too unfavourable a light the influence of old age *per se*. C. L.

Marsiglia, G. Le secrezioni interne e il retardo di consolidazione delle fratture. [**Internal secretions and retarded consolidation of fractures.**] *Arch. ital. di chir.*, 1922, **5**, 197.

The author sums up previous work on the subject thus: Various researches on different glands all relate to young animals still developing; thyroidectomy, it is agreed, produces some delay in consolidation; thymectomy, not only delay but actual defect; parathyroidectomy, even partial, according to some, leads to delay, whilst others observe no effect; removal of the suprarenals, unless bilateral and therefore incompatible with life, exerts no influence on repair; oophorectomy slightly accelerates callus formation.

Marsiglia has repeated the experiments on adult dogs, fracturing a leg two or three days after the ablation of the gland, and using controls. Thyroidectomy, partial or complete, causes no delay, though in some cases there seemed to be rather a large mass of callus which was absorbed but slowly; the osteoid phase lasted longer than in the controls. Parathyroidectomy he found technically impracticable. Unilateral suprarenal removal produced no effect; uni- or bi-lateral oophorectomy had no influence. Complete removal of the pituitary in dogs the author found impracticable by any route, but by the external orbital approach, using a calibrated instrument, he was able to pulp the gland in such fashion that at the post-mortem forty days later the tissue was found necrotic. Repair of the fractures was unaffected. Histological examination of all the fractures revealed nothing for remark.

It is probable, therefore, that there is no one gland, even in man, that has any effect on the course of callus formation, or on the causation of non-union or pseudarthrosis; or that the administration of extracts of one or more of the endocrine glands will have any value, at any rate in the adult. E. R. C.

St. John, V. Tuberculosis of the flat bones of the skull. *Brit. J. Surg.*, 1921, **9**, 228–34.

Cranial tuberculosis is rare, although St. John believes it less rare than is usually thought. The author takes as his text four cases seen by him in 1919 and 1920. Pelletier had collected 206 cases in 1910 and Wieting and Raif 10 others in the same year. The condition is generally associated with other tuberculous lesions elsewhere, especially in bones and joints, but may

be isolated; of the author's four cases two had multiple lesions, one pulmonary tuberculosis, and in the other there was no other discoverable tuberculous lesion at the time of observation. The disease affects children and adolescents particularly, but may be seen in adults; in 161 of Pelletier's cases 128 were under 20, 19 between 20 and 30, and 14 over 30. The bone involved is usually the frontal or parietal; much more rarely it is the temporal or occipital.

Two varieties have been distinguished, namely, the perforating form and the diffuse, progressively infiltrating form; the perforation may be single but is more often multiple. The author, however, does not approve a definite distinction between the two forms of the disease because the perforations, if multiple, do not indicate separate foci. They are in communication through the diploe, and the disease, circumscribed at first, in the later stages is diffuse. The tuberculous infiltration begins in the cancellous tissue of the diploe; later it may affect chiefly the outer or chiefly the inner table. The author in his cases found the external table the more extensively involved. When the sequestrum is total it may invade a larger area of external table, and then has a tendency to spontaneous separation and elimination. If the inner table is chiefly necrosed the sequestrum is shut in and cannot extrude itself. A cold abscess is formed under the periosteum and is confined by it at first, but later it perforates this membrane and spreads widely in the scalp; then it may open externally and a probe may feel a sequestrum or may go straight down to the dura mater. The dura shows external pachymeningitis and does not pulsate normally; the dura may be covered with granulations over a wide area. A true extradural abscess is rare. In one case the author saw invasion of the frontal sinus; he cites another (Panse), in which caries of the orbit and accessory nasal cavities occurred. Tuberculous meningitis is uncommon; Delamare and Conor note 1 case in 15, and Pelletier in 206 cases found 9 with meningitis and 4 with cerebral tuberculoma.

The cold abscess is the chief diagnostic point. Headache is infrequent and in this the disease differs from syphilis of cranial bones. In syphilis the bone is worm-eaten, the sequestra are hard, and the surrounding bone is thick; in tuberculosis the sequestra are friable, the surrounding bone is of normal thickness, and the periosteum is not thickened but is perhaps in places separated from the bone by a layer of granulations.

The treatment is surgical. The tuberculous processes must be followed to their full extent, and the tracks in the bone laid open; they must then be thoroughly cleaned out and the scalp sutured. Operation must be repeated if necessary. The prognosis depends on the lesions elsewhere; isolated cases usually recover. C. C. C.

Cushing, Harvey. A large epidermal cholesteatoma of the parieto-temporal region deforming the left hemisphere without cerebral symptoms. *Surg. Gynec. & Obst.*, 1922, **34**, 557–66.

These tumours, though fairly common in the temporal region, usually excite considerable comment when discovered *post mortem* in other parts of cranium. They have never been diagnosed before operation or autopsy. They were first spoken of by Cruveilhier as 'tumeur perlee'. They were given their present name in 1838 by Johannes Mueller. The term has been used since to describe any tumour which contains cholesterin crystals,

whether of endothelial or epithelial origin. Those of epithelial origin are found to be less than 1 per cent. of intracranial neoplasms. In the author's 740 cases of tumours there were only three examples of cholesteatoma. In two cases hair was present in the tumour, so they may arise by epidermal or dermal implantation. The most common situations are (1) in and about the temporal bone, (2) free in the leptomeninges of the cerebral base, (3) the cerebral ventricles, these last being endothelial tumours. They also occur between the two tables of the skull, their glistening surface obscured by their environment. As they grow the inner table becomes ballooned out and absorbed more than the outer.

In the cases described there were few signs—a slight dragging of the left foot, weakness of the left hand, homolateral signs difficult to explain, with very definite X-ray signs over the left hemisphere. This consisted in a quadrilateral area of absorption of bone about 3·5 inches on each side, the outline sharply demarcated; at one point there was complete absorption which corresponded to a tender and pulsating spot in the skull. An osteoplastic flap operation was performed, the margins of the flap being outside the absorbed bone. The tumour was stripped away from the bone, leaving a large depression in the hemisphere. The tumour weighed 175 gm. and measured 4 inches in diameter.

Six historical cases are quoted of this diploic type of cholesteatoma where operations had been performed by opening into the tumour, through the absorbed bone making the proper eradication of the tumour extremely difficult, as the important thing is completely to remove the epidermal membrane if recurrence is not to take place, and this is wellnigh impossible if the cyst has collapsed. J. B. H.

Mygind, H. Den akute Mellemöresuppurations kirurgiske Komplikationer belyste ved 1000 Mastoidaloperationer. [**The surgical complications of acute middle ear suppuration illustrated by 1,000 mastoid operations.**] *Hosp.-Tid.*, 1922, **65**, 40.

Mygind has prepared a statistical analysis of 1,000 mastoid operations on 830 patients between 1905 and 1920. In 95 cases both sides were operated on, and in 83 the operations were for relapses. With regard to aetiology, he found influenza play a most important part, and in the overwhelming majority of cases a bacteriological examination of the pus in the mastoid process showed streptococci; the mortality among the streptococcal cases was comparatively high. Only in 4 per cent. was the middle ear disease unaccompanied by osteitis of the mastoid, and in most of these cases there were endocranial complications occurring without osteitis of the mastoid as a link between the middle ear and the endocranial disease. Only in 1·4 per cent. of the children operated on were tubercle bacilli found on microscopic examination of the pus; but in several cases the pale and indolent granulations, and the colloidal appearance of the pus in the mastoid process suggested a tuberculous aetiology even in the absence of bacteriological evidence. With regard to treatment, opening up the mastoid is not indicated when, as often happens in the early stage of acute suppurative middle ear disease, periostitis of the mastoid with considerable swelling develops. On the other hand, periosteal swelling, which occurs at a later stage, or which persists beyond the first stage, is a sign that osteitis of the mastoid itself has occurred, requiring radical treatment. Mastoid periostitis frequently

terminates in suppuration with the formation of a subperiosteal abscess; this was found in about about one-third of all the cases and was thrice as frequent among children as among adults. The absence of periosteal swelling of the mastoid in cases with intracranial complications was often striking. Of the four most important and frequently fatal intracranial complications (meningitis, thrombophlebitis, brain abscess, and subdural abscess) thrombophlebitis occurred in 5·2 per cent. of all the cases and was almost twice as frequent among adults as among children. Recovery occurred in 60 per cent., and among children thrombophlebitis terminated in recovery in 70 per cent. The prognosis was particularly favourable in cases of otogenous thrombophlebitis complicated by metastatic lesions in the joints, tendon-sheaths, bursae, and the like, none of the 7 patients with such metastases dying. But metastases in the lungs proved almost invariably fatal. In 6 per cent. of the children and 9 per cent. of the adults there were signs of meningitis before the operation; post-operative meningitis developed in 3 children, 2 of whom recovered, and in 5 adults, all of whom died. Recovery from meningitis occurred in 46 per cent. of the children and only in 10·5 per cent. of the adults. The prognosis was very bad for meningitis due to chronic middle ear suppuration.

Discussing his high mortality-rate among infants and young children, Mygind notes that most of the fatal cases in this class were represented by weakly, tuberculous, rachitic, or atrophic children. Among otherwise healthy children suffering from osteitis of the mastoid without intracranial complications, there were only 8 post-operative deaths (1·6 per cent.). Death in 7 of these cases was due to pneumonia. The aetiology of post-operative brain complications is usually obscure, particularly when they occur several weeks after the operation; occasionally accidental injury to the sigmoid sinus and dura mater in the course of the operation is to blame.

C. L.

Schmiegelow, E. Den akute Mellemöresuppurations kirurgiske Komplikationer. [**The surgical complications of acute middle ear suppuration.**] *Hosp.-Tid.*, 1922, **65**, 45.

Schmiegelow has operated on 801 cases of middle ear suppuration in the period 1900–20 and has found that endocranial complications were far less frequent in his material than in Mygind's. Pyaemia and thrombosis occurred only in 2·3 per cent., and among his cases of chronic middle ear suppuration sinus thrombosis with pyaemia occurred only in 1·3 per cent. Eight patients developed an epidural abscess, 2 a subdural abscess, and 5 a perisinus abscess. Meningitis was observed in 22 cases. Schmiegelow publishes these figures with the reservation that such statistical analyses give very imperfect information and are apt to be misleading. C. L.

Crile, Geo. W., and **Lower, W. E. Special points in the technic of operations on the thyroid gland.** *Ann. Surg.*, 1922, **75**, 47.

The amount of gland to be left depends entirely on the type of goitre. In exophthalmic the amount is small and in colloid goitre the amount must be larger in order that the function of the gland may be carried on. For cosmetic reasons it is better not to leave the poles or the isthmus. The writers advocate the high division of the preglandular muscles as giving better access, but in certain cases state that transverse division

only will give the necessary exposure. Separation of the true capsule is not advised, as it is found that the recurrent laryngeal is frequently involved later in scar-tissues. The turning out of the gland with the fore-finger should not be done until such time as the poles are freed; especially is this so in bilateral deep goitres, as there is danger of bilateral paralysis of the recurrent necessitating immediate tracheotomy. Care should be taken that when vessels are ligated on the surface of the trachea the peritracheal fascia is not included, as this may involve the sensory nerves to the trachea and their constant irritation may give rise to increased mucus and to a local tracheitis probably followed by a broncho-pneumonia.

In cases of respiratory obstruction during operation tracheotomy is advised and as soon as the obstruction is removed the trachea should be closed. Care should be taken, if this is done, that no blood is inhaled. Delayed closure in serious cases is recommended, the whole wound being left open and dressed with 1–5,000 flavine. It is closed under local anaesthetic either the same day or the next. It is claimed for this that the danger of hyperpyrexia is greatly lessened. If, at any time during an operation, there appears to be any doubt as to the outcome, the wound should be packed with flavine and the operation stopped, to be concluded at a later date.

Although the authors design their pre-operative technique so that the ordinary patient is unaware of the day or hour of operation, no stress is laid on deceiving the patient as to time of operation, if she desires the information; if in consequence of receiving it the patient's condition becomes unsatisfactory, then the operation is postponed.

The value of X-rays in reducing thyroid secretion is not disputed, but, owing to the difficulty in dosage, it is not advised.

Ligation of the arteries is carried out as a preliminary to thyroidectomy and the authors believe that the immediate benefit that occurs is due to the break in the sympathetic nerve-supply that runs along the vessels, and is not due to the diminished blood-supply.

The writers hold that the indication for thyroidectomy is the diagnosis of hyperthyroidism and that, as in appendicitis, the rule 'operate on diagnosis' should apply. J. B. H.

Vaccari, C. Sulla reazione dei tessuti animali alla introduzione di spugna e di lamina di gomma. [**On the reaction of animal tissues to the introduction of rubber sponge and sheet.**] *Arch. ital. di chir.*, 1922, **5**, 117.

This interesting and careful research, conducted almost exclusively on rabbits, gives results much as might have been expected. Rubber does not differ appreciably from other substances such as marine sponge, paraffin, pith, cork, or metals, in the tissue-reaction and encapsulation it excites. Rubber-sponge by its structure lends itself admirably to penetration by connective tissue, and it is possible that the sulphates of zinc, barium, and calcium liberated by the partial but continuous disintegration of the rubber, maintain a steady stimulus which results in the persistence, certainly for many months, of highly cellular 'young' tissue, richly vascularized. The cells met with include those of granulation tissue, with eosinophils having a single reniform or round nucleus; large and small pigmentiferous cells which are found so crowded with rubber particles as to have their nuclei obscured; and epithelioid cells identical with the

'Eiterphagocyten' of Maximow. The elastic properties of the rubber have practically no influence and indeed tend to be early lost.

Pieces of rubber-sponge, sterilized by half an hour's boiling, introduced into the peritoneal cavity, are simply encysted, sometimes with formation of adhesions. The shape of the piece may be altered by compression, folding, or elongation. Similar results are found when the sponge is embedded in muscle; it becomes ensheathed and interpenetrated by connective tissue continuous with that of the host tissues, but there is, of course, no stimulation of muscle-cells proper, to new formation.

Some of the most interesting experiments were those in which a part, or the whole, thickness of the abdominal wall were replaced with rubber-sponge of the same size as the portion removed. With successful fixation there was no herniation, though this often occurred from failure of the retaining sutures. The connective-tissue mass enclosing and permeating the rubber (most of the bulk of which remained after eight or nine months) made a very competent cicatrix. It is curious that the surface towards the viscera though covered with a fibrous film of smooth texture, apparently showed no sign of endothelialization. The results support the clinical experience of Delbet and others that a sheet of rubber-sponge may be satisfactorily employed to reinforce a feeble abdominal wall in the cure of large ventral and similar herniae. It may serve a similar purpose as the groundwork of plastic repair of the thoracic wall. The author also employed rubber-sponge and strips of rubber-sheet to effect nephrorrhaphy, enclosing the organ in a kind of net or open bag with tags for attachment to muscle or fascia. The web of fibrous tissue resulting forms a competent retainer with more extensive and intimate adhesions than would have resulted without its use.

In bone cavities it serves no purpose beyond filling the space; there is inhibition rather than stimulation of bone formation, and complete preliminary sterilization of the cavity is necessary if the rubber be not to extrude or call for removal. E. R. C.

NEUROLOGY

Goldman, A. Clinical tetany by forced respiration. *J. Am. M. Ass.*, 1922, **78**, 1193.

In a previous number of *Medical Science* the artificial production of the symptom-complex of tetany by forced respiration was discussed (1921, **3**, 427). Goldman reported the phenomenon in a series of medical students, who carried out forced breathing for a period of two minutes. In the present paper he records the clinical occurrence of the symptom-complex in eleven cases: (1) A medical student suffered from gall-stones and cholecystitis, and during several attacks of severe pain with fever and prostration he began unwittingly to breathe deeply. The symptoms of tetany developed and were diagnosed as being epileptiform attacks. The student, having seen artificially-produced tetany in the students above mentioned, himself recognized the nature of his condition. (2) A nurse, while walking, felt faint and sick and short of breath. She continued to breathe deeply as

she felt she could not get her breath quickly enough. Ten minutes after the onset of these symptoms she was examined. There were typical carpo-pedal spasm and positive Trousseau and Chvostek signs. She was diagnosed as tetany from over-ventilation. (3 and 4) Two similar cases of patients who, in hysterical attacks, breathed deeply and developed clinical tetany. (5) A case of acute pharyngitis, laryngitis, and bronchitis. Periodically there were attacks of deep rapid breathing, followed in each case by the development of symptoms of tetany. (6) Attacks of deep breathing during an influenzal infection, with the development of symptoms of tetany. (7–11) Five students who developed tetany during the forced breathing following violent physical exercise. In several of these cases, the urine examined during the attack was strongly alkaline. The author quotes Barnes's classification of tetany; infantile, following removal of the parathyroids, during pregnancy and lactation, associated with gastro-intestinal disorders, in acute fevers, following poisoning by chloroform, morphia, ergot, lead, and alcohol. Other authors also give exercise, excitement, and hysteria as causes. Goldman believes that in many of these cases over-ventilation with resultant alkalosis is the essential cause. F. M. R. W.

Morris, N. Anoxaemia and the increased electrical excitability of the neuro-myone. *Brit. J. Exper. Pathol.*, 1922, **3**, 101.

Increased electrical excitability of the peripheral neuro-muscular mechanism has long been known to occur in idiopathic tetany and in tetania parathyreopriva. Experimental investigations have indicated that this change has its seat peripherally, and numerous theories have been propounded to explain its occurrence. Excess of sodium in the blood, decrease in the calcium content of the organism, alkalosis, acidosis, or the presence of a toxic substance in the blood have all been invoked in explanation. The object of the investigation recorded in the present paper has been to throw more light upon this subject. Using standardized electrical stimuli, the electrical reactions of the muscles of anaesthetized cats and dogs were examined.

Morris reviews the work upon which the theories mentioned above have been based. His conclusions include the following: Any experimental method productive of anoxaemia causes an increase in the electrical excitability. Any increase in the electrical excitability is accompanied by diminished oxygen supply to the tissues. We must, therefore, conclude that anoxaemia is the essential condition underlying an increased electrical excitability of the peripheral neuromuscular mechanism.

These observations are of interest to neurologists in view of the clinical findings reported by Goldman and abstracted in this number of *Medical Science*, and of the considerations discussed in a review on anoxaemia in this journal (1921, **4**, 427), and it is possible that their bearing on neurological problems may, with advance in knowledge, prove to be still wider than is at present apparent. F. M. R. W.

Woods, A. H. Occipital lobe embolism. *J. Nerv. & Ment. Dis.*, 1922, **55**, 81.

The origin of cerebral emboli is discussed. Bone disease in the neighbourhood of an artery favours thrombosis and embolus formation. In

passing through the costo-transverse foramina of the upper cervical vertebrae, and in winding round the articular process of the atlas, the vertebral artery is almost inevitably involved in a small area of osteoperiostitis of that region. The walls of blood-vessels, like the dura mater, resist invasion by infective processes, yet organisms penetrate the vessel wall by way of the lymphatics and thus gain the intima, causing a local inflammatory reaction, which may result in occlusion of the lumen. Thus a possible source of embolism arises. A case is recorded in which this is thought to have been the order of events. A woman of 30 suffered from pain and stiffness in the left side of the neck. While receiving passive movements of the neck at the hands of an osteopath, the patient's left limbs suddenly became numb and 'felt asleep'. In addition, the subjective sensations were accompanied by weakness and clumsiness of the affected limbs. At the moment of onset, also, the patient became aware of 'a dense black shadow obscuring everything on the right side'. Examination ten weeks later revealed an homonymous upper quadrantic hemianopia on the right, the scotoma extending up to the zero point. No objective motor or sensory symptoms were found, and there was no definite alteration of the reflexes. Pressure over the left second and third transverse processes of the cervical vertebrae was painful, and the surrounding soft tissues showed an increased resistance on palpation. Movements of the head were painful. Radiography revealed a deepening of the normal shadow in the region of the left side of the atlas and axis. A second case of occipital lobe embolism in a man with endocarditis is described, in which, in addition to hemianopia, there was some disorientation, so that the patient had difficulty in finding his way home.

Woods supposes that in the first case an embolus lodged in the artery supplying the lower half of the area striata of the occipital cortex, and in the second in the main stem of the posterior cerebral artery. The author discusses these visual symptoms in the light of Gordon Holmes's work upon the cortical representation of vision, with which his observations agree (cf. *Medical Science*, 1920, **2**, 65). F. M. R. W.

Guillain, G. (1). Sur un cas de tumeur du splénium du corps calleux. Contribution à l'étude sémiologique des tumeurs du corps calleux. [B.] [**A case of tumour of the splenium of the corpus callosum. Contribution to the study of the symptomatology of corpus callosum tumours.**] *Ann. de méd.*, 1922, **11**, 33.

Guillain, G. (2). Sur un cas de tumeur du splénium du corps calleux. [**Tumour of the splenium of the corpus callosum.**] *Rev. neurol.*, 1922, **i**, 20.

In the *Annales de Médecine*, Guillain gives a review of the clinical literature of tumours of the corpus callosum. Duret (1905) appears to have been the first to attempt to differentiate the symptom-complexes of the corpus callosum according to whether the anterior, middle, or posterior part was involved. Characteristic of all corpus callosum tumours, according to this observer, are bilateral motor weakness, predominating on one side, an absence of signs of involvement of cranial nerves at the base of the brain, and an absence of sensory changes. In tumours of the genu or anterior part, psychical disturbances are early and prominent (stupor, confusion, and dementia). Defects of speech—dysarthria and motor aphasia—and Jacksonian attacks in the muscles of the face, tongue, neck, and upper

limbs are also frequent. When the mid part is involved the same bilateral unequal motor weakness is seen, with titubation and astasia-abasia. Finally, in lesions of the splenium, the motor weakness is said to predominate in the lower limbs and to be associated with visual disturbances and ataxy of cerebellar type. Raymond (1906), discussing the mental changes, regards progressive mental deterioration as characteristic of genu tumours, and delirium and excitability of splenium lesions. Often the change in the patient's character suggested the presence of general paralysis. Raymond, Lejonne, and Lhermitte (1906) believe that mental change is the only pure corpus callosum symptom, and consists in a loss of association of ideas, eccentricities of behaviour, defect of memory, especially for recent events, irritability and capriciousness, without actual delirium. In short, from a review of the extensive literature on the subject, it appears that tumours of the corpus callosum present a characteristic clinical picture in which progressive dementia and hebetude are early and prominent symptoms, apraxia is common, slight bilateral hemiplegia predominating on one side and often associated with tremor and some ataxy is the rule, while the ordinary signs of increased intracranial tension, headache, vomiting, and papilloedema are later in development and tend to be less severe than in tumours elsewhere in the brain. In respect of tumours of the splenium, Guillain gives the following special symptom-complex: (i) General signs of intracranial tension occur, but are less marked than is common in cerebral tumours. (ii) Psychical disorders, such as amnesia, disorientation and confusion, emotional apathy with alternating stupor and agitation. (iii) The frequent presence of motor symptoms, bilateral weakness and spasticity, which are really due to compression of the adjacent motor paths. (iv) The occasional presence of apraxia. (v) Absence of aphasia. (vi) The absence of cranial nerve palsies. In both papers he records a case of tumour involving the splenium bilaterally. The patient was a man of 52 who, eight months before coming under observation, was first noticed to be changing mentally. His memory became uncertain and he made mistakes in his accounts. He suffered from violent headache and giddiness. The fundus oculi was not examined. There were no cranial nerve palsies, nor any motor symptoms. The tendon-jerks in the upper limbs were feeble and in the lower limbs were abolished. Abdominal and plantar reflexes were absent on both sides. The pupils were unequal and reacted feebly to light and to accommodation. The patient's memory was grossly defective, he could not remember his address, nor the events of the day, and was unequal to the smallest calculation. He was not paralysed, but was unable to carry out even the simplest acts; there was marked apraxia. Examined just before death, he was somnolent, showed gross loss of association of ideas, and had periodical accesses of excitement, in which he wandered about, with some ataxy, and, from his profound loss of vision, was constantly knocking into the objects in the room. There was no paralysis, apraxia could not be investigated, but there was a fine tremor of the right hand. Lumbar puncture revealed a clear fluid under pressure, yellow in colour, free from excess of cells but rich in globulin (xanthochromia). Death occurred ten months from the first appearance of symptoms. Autopsy revealed a glioma infiltrating the splenium on both sides and just beginning to involve the thalamus on the left. F. M. R. W.

Souques, Alajouanne, et Bertrand. Tumeur primitive du septum lucidum avec troubles démentiels. [**Tumour arising in the septum lucidum, with symptoms of dementia.**] *Rev. neurol.*, 1922, i, 270.

The patient was a woman of 41, who entered hospital in a state of dementia. No history of her malady was available, and no diagnosis of cerebral tumour was made during life. She was completely disoriented as to time and place, and was unable to answer the simplest questions relative to her own past life or to current events of public interest. There was no defect of speech, either of comprehension or of expression, within the narrow limits allowed by her mental state. There was incontinence of urine. No mention is made of the state of the fundi of the eyes. The cranial nerves were normal apart from inequality of the pupils, the left being the larger with loss of reaction to light, the light reaction in the right was feeble, and there was slight tremor of the tongue. The patient walked slowly and tended to drag her feet. There was slight extensor rigidity of the legs. There was no weakness. No sensory loss was detected. All the reflexes were normal. The patient became slowly more demented, and died comatose with pulmonary symptoms six months after admission to hospital. Mesial sagittal section of the brain revealed the presence of a tumour, the size of a hen's egg, situated in the septum lucidum. Anteriorly, it reached to the level of the genu of the corpus callosum, and posteriorly insinuated itself between the corpus callosum and the pineal body. The lateral ventricles were widely dilated, but the third ventricle was reduced to a slit. Microscopically, the tumour proved to be a glioma undergoing cystic and calcareous degeneration.

The authors have found two similar cases recorded in the literature, but no details of these are given. On the other hand, the spread of growths arising in the corpus callosum to the septum lucidum is known to occur. They believe that the concurrence of three factors in their case, namely, compression of the corpus callosum, hydrocephalus, and compression of the cerebral cortex, account for the profound dementia, though they do not attempt to estimate the relative importance of these. F. M. R. W.

Rehn, E. Myoelektrische Untersuchungen bei Striatumerkrankungen. [**Electromyographic studies in diseases of the corpus striatum.**] *Klin. Wchnschr.*, 1922, **1**, 673.

Gregor and Schilder have reported that the muscular rigidity of paralysis agitans is not accompanied by any current of action in the muscles, and have used the observation as an argument in favour of a supposed dual function of striated muscle, phasic and tonic contraction. They employed non-polarizable electrodes applied to the skin over the muscle to be tested. Rehn has repeated their observations, using needle electrodes piercing the skin and applied directly to the muscle. He finds that there is a continuous electrical response in the muscle, indicating that the rigidity and the tremor of patients with paralysis agitans and other diseases of the corpus striatum is of the nature of a tetanus. In two cases of post-encephalitic paralysis agitans with rigidity and tremor, he took leads from deltoid and biceps at moments when no tremor was visible. The record revealed oscillations of two types with a rhythm of 45–50 per second, waves of small amplitude, and at a rate of 6 per second waves of large amplitude (synchronous with the clinically observed tremor, although no tremor was

seen at the time). When a voluntary movement was made, both types were merged in the large oscillations of voluntary innervation. However, the rhythm was not interrupted, but remained constant—that is, 45–50 per second. In a second, the original two-wave oscillations appeared again and continued.

In the sternomastoid of one of these patients, uniformly large oscillations of the same rhythm occurred, without the small intercalated waves described above. The same was found in the pectoralis of a case of torsion spasm, but in the flexores carpi ulnaris et radialis of this patient a third form of record was obtained. A series of waves of large amplitude lasted for $\frac{3}{4}$ to $1\frac{1}{4}$ sec. and then gave place to small oscillations for a similar period—that is, groups of large and of small waves alternated.

The interesting fact emerges from these observations that the tremor and rigidity give records characteristic of a tetanus, and differ from each other and from the record of voluntary innervation, not in character, but simply in amplitude, the rhythm in each instance being the same. A similar large wave-curve was obtained from a case of spastic diplegia. Further investigations are in progress.

These observations appear to give no support to the view that tonic muscular contraction is subserved by a special muscular apparatus. In respect of these observations it must be remembered that the interpretation of electromyograms is beset with pitfalls. The small oscillations described by Rehn are to be found in almost every electrocardiogram, and probably arise in the skeletal musculature and not in the heart-muscle, Their amplitude in these circumstances is the resultant of several factors. When the subject is in an uncomfortable posture, is cold or apprehensive, they tend to be more marked than when he is completely in repose, warm, and free from emotional reaction, but they are seldom entirely absent. We cannot, therefore, accept as finally determined the nature and significance of these records. Whether they are directly associated with the rigidity of striatum diseases remains doubtful. F. M. R. W.

Foix, Ch., et **Fatou, E.** Syringomyélie a début par cypho-scoliose juvénile, apparition tardive des accidents confirmatifs. [**Kypho-scoliosis as the initial symptom in syringomyelia.**] *Rev. neurol.*, 1922, i, 28.

The authors describe two cases of syringomyelia, in both of which kypho-scoliosis was present for several years before the onset of signs of spinal cord lesion. In one the spinal curve had developed painlessly and without other symptoms at the age of 15. At the age of 28 spastic paresis of the right leg developed. Examination revealed symptoms of a syringomyelic cavity extending throughout the length of the thoracic cord and almost entirely right-sided. There was no wasting of the upper limbs and the spinal curve had its convexity directed to the right.

The second case was that of a man of 52 who came under observation for chronic bronchitis, and who was found to have a kypho-scoliosis of the thoracic spine, convex to the right. The patient was not aware of any symptoms referable to the nervous system, and stated that the spinal curvature had developed painlessly and as an isolated symptom at the age of 15 years. Examination revealed sensory loss of dissociated character corresponding to the whole extent of the thoracic cord and mainly right-sided. Beyond the presence of increased tendon-jerks and a Babinski type

of plantar response on the right side, there were no other physical signs. In short, the syringomyelia was latent, except for the spinal curvature.

The authors point out that both cases showed unilateral lesions of the thoracic cord, and that the convexity of the scoliosis pointed to the side of the lesion.

They believe that weakness and dystrophy of the erector spinae on the right side had allowed the intact muscles of the left side to act unopposed and thus to produce the curve.

Radiographic examination of the spine revealed no abnormality of the vertebrae, and they reject primary trophic lesion of the bone as the cause of the kypho-scoliosis. F. M. R. W.

Souques, M. A. Un cas de paralysie agitante conjugale. [**Conjugal paralysis agitans.**] *Rev. neurol.*, 1922, i, 302.

The observation is of interest when read in connexion with the statistics of post-encephalitic paralysis agitans recorded by Grossman and described in *Medical Science* recently (1922, **6**, 311).

The wife, aged 52, was taken with an acute febrile illness in July 1919. The disturbance was transient (she was confined to bed for two days only) and consisted in fever, amblyopia, and vertigo. Six months later she had a relapse, with persistent insomnia and the development of the clinical picture of paralysis agitans without tremor. The husband, aged 65, since January 1920 has had an intermittent tremor of Parkinsonian type in the left arm. In both instances the symptoms are progressive. Souques regards both as examples of a post-encephalitic nervous lesion, though in the case of the husband the initial infection passed unnoticed. He gives figures relative to 102 cases of post-encephalitic nervous symptoms. Of this series, a symptomatic paralysis agitans was present in 71, choreiform and 'myoclonic' involuntary movements in 18, cerebellar symptoms in 3, neurasthenic states in 3, and psychical disturbances in 7. In two-thirds of his cases, therefore, the clinical picture of paralysis agitans developed.
F. M. R. W.

Holmes, W. Relation of increased blood viscosity to transient attacks of hemiplegia. *J. Am. M. Ass.*, 1921, **76**, 1640–2.

Holmes admits that it is difficult to prove either the angiospastic or any other theory of transient hemiplegia, but quotes two cases in which it occurred after incidents which may be supposed to have led to loss of fluid from the body. This in turn would tend to concentrate the blood, increase its viscosity, and so possibly lead to a temporary cessation of circulation through parts of the brain. He quotes as also in favour of his views the observation that intermittent claudication is much relieved by forcible administration of fluids, and mentions as favouring the occurrence of these hemiplegias the fact that elderly persons often restrict their intake of fluid owing to prostatic troubles. G. W.

Hassin, G. B. Histopathologic findings in a case of superior and inferior polioencephalitis with remarks on the cerebrospinal fluid. *Arch. Neurol. & Psych.*, 1921, **5**, 552.

The patient, a man of 21 years of age, showed imbecility, loss of spatial sense, marked paralysis of the 3rd, 4th, 5th, 6th, 7th, 9th, and 12th

cranial nerves, with partial involvement of the 10th and 11th nerves on both sides. The spinal fluid was under normal tension, colourless, with five lymphocytes per c.mm. and a negative Nonne test. Two days after his admission to hospital he suddenly died. The diagnosis was imbecility, polio-encephalitis superior and inferior. At the autopsy the brain only could be removed. The pia mater was smooth, easily detachable from the brain, and shiny, except the portion over both occipito-parietal regions, which showed marked haemorrhages. The convolutions were of normal size, and were not flattened: the sulci were of usual depth. The grey matter of the midbrain and medulla appeared unusually dark — almost black—sharply contrasting with the surrounding white substance. Macroscopic haemorrhages or foci of softening were absent; the ventricles were not enlarged and there was no proliferation of the ependyma. On microscopic examination the main pathological changes were found, as expected, in the midbrain and medulla. In these regions a remarkable degree of congestion was observed, the blood-vessels being noticeably distended while the smallest capillaries were unusually prominent and engorged with blood. A new formation of capillaries was also frequently noticed. In the basal ganglia, especially in the lenticular nucleus, the vascular walls sometimes showed proliferation of adventitial and endothelial cells with an abundance of brownish-green, round granules. In some instances, erythrocytes were seen scattered freely in the nervous tissue or enclosed within various gliogenous formations. Similar vascular changes were found in the cortical layers, especially in the occipital lobes, to a lesser extent in the cerebellum, and quite pronounced in the choroid plexus. While no perivascular infiltration could be detected, a characteristic feature was the almost universal presence of great quantities of fat granules within or around the vessel walls, including those of the smallest capillaries. The nerve-cells sometimes appeared quite normal even in those parts of the midbrain which exhibited structural changes in the glia and blood-vessels. Other nerve-cells showed undoubted pathological changes, such as chromatolysis, displacement of the nucleus, sclerosis, atrophy, with a more or less remarkable degree of so-called neuronophagia. Stained with scarlet red, these altered cells showed an abundance of fat drops throughout the entire cell body. The foregoing cellular changes were particularly marked round the third and fourth ventricle and the Sylvian aqueduct, involving the nuclei of all cranial nerves from the 3rd to the 12th pair, including the locus coeruleus. Marked as these changes were, much more striking was the presence of a very great number of 'gitter' cells of the varieties α, β, and γ of Jacob (*Histol. u. histopath. Arb. über d. Grosshirnrinde*, 1912, **5**, 1). They were particularly abundant around capillaries and smaller vessels apparently in those regions which were most affected, as well as in the subarachnoid spaces, where they were mixed with 'mesothelial cells' and red blood corpuscles. The neuroglia showed many signs of active proliferation, particularly characterized in the midbrain and medulla oblongata by the presence of many protoplasmic glia cells. Noteworthy changes were also found in the choroid plexus. The vessels were engorged, the endothelial and adventitial cells of the capillaries prominent while the epithelial cells appeared as 'unusually large, expanded reticular bodies' and contained a great number of fat droplets. The nerve-fibres were frequently poorly stained, sometimes swollen and irregular in shape, or broken into fragments, stainable by Marchi's method. These findings

led the author to the conclusion that polio-encephalitis superior of Wernicke is not an inflammatory, but a partial manifestation of a general degenerative process of the central nervous system, and that it is analogous to other degenerative processes such as amyotrophic lateral sclerosis, subacute combined cord degeneration, &c., from which it differs by the localization of the degenerative phenomena. With reference to the presence of 'gitter' cells in the pia-arachnoid and subarachnoidal spaces and to the changes found in the choroid plexus, Hassin puts forward the following suggestion: 'The subarachnoid space is a receptacle of the tissue fluids which carry away the waste products of the brain. The function of the choroid plexus is probably to pick up from the cerebrospinal fluid harmful or other products and to render them, as well as the fluid, more absorbable.' C. d. F.

Thalhimer. Epidemic (lethargic) encephalitis. *Arch. Neurol. & Psych.*, 1921, **5**, 113.

For his cultural and experimental investigations Thalhimer obtained material from four cases of epidemic encephalitis, two of the 'fulminating type', one with marked 'myoclonus' and one showing lethargy. The central nervous system of all had the characteristic lesions of the disease, such as capillary congestion, microscopic haemorrhages, perivascular mononuclear leucocytic infiltrations, microscopic areas of degeneration and necrosis. The two fulminating cases showed marked congestion, great numbers of capillary haemorrhages, a few areas of localized necrosis with round cell infiltration and here and there slight or marked perivascular round cell infiltration. The other two cases, which ran a longer clinical course, also showed all these lesions, but many, instead of a few, of the vessels were surrounded by round cells. The degree of this perivascular infiltration was also greater. Cerebrospinal fluid was obtained from one of the fulminating cases and from a convalescent patient who had manifested marked lethargy and still had, at the time of lumbar puncture, headache, nausea, vomiting, and a slow pulse. With this material a number of guinea-pigs and about 200 rabbits were inoculated intracranially according to the method devised by Loewe. Cultures were made by means of the ascitic fluid tissue medium as perfected by Noguchi. The results obtained were identical with those reported by Loewe and Strauss and confirmatory of both their animal experiments and cultural studies. The author is therefore of the opinion that an infectious agent has been demonstrated which is apparently constantly associated with epidemic encephalitis. This infectious agent passes through a porcelain filter capable of holding back *B. prodigiosus*, the filtrate producing a disease in rabbits which is very similar to lethargic encephalitis and is characterized by microscopic brain lesions identical with those found in fatal human cases. The disease is transmissible in series from animal to animal even when the brain emulsions prepared for inoculation purposes are filtered through a Mandler porcelain filter after each animal passage. The infectious agent, which was grown from the brains of about 80 per cent. of the rabbits inoculated with filtered virus, stains a violet-blue with methylene blue and purplish with Giemsa's fluid. It is extremely minute, rounded, and measures from one-fourth to one-fifth of the diameter of a small anhaemolytic streptococcus. It is found singly, in pairs, in short chains, and groups, and stands out

sharply by the usual magnification of an oil immersion lens. Cultures of this micro-organism, when inoculated intracranially into rabbits, cause the same disease and the same brain lesions as the filtered brain emulsions from human cases, or successfully infected animals, and the same organism can be recovered from the central nervous system of rabbits inoculated with cultures. It is therefore believed to be the aetiologic agent of epidemic encephalitis. C. d. F.

Campora, G. Sopra un caso di emicorea con reperto necroscopico. [**A case of hemichorea with post-mortem examination.**] *Pathologica*, 1922, **14**, 41.

A hemichoreic syndrome was observed in a woman 70 years of age. The choreic movements began suddenly, were limited to the left side of the body, and lasted for a month, ceasing only one hour before death. At the post-mortem examination of the brain nothing abnormal was found but a relatively recent haemorrhagic cyst occupying, and in part destroying, the right hypothalamic nucleus. By means of transverse vertical sections (Déjerine's method), it was ascertained that the lesion extended ventro-dorsally from the anterior end of Luys's nucleus to the capsule of the red nucleus; laterally almost to the posterior segment of the internal capsule; mesially to Forel's area, ending about 3 mm. from the median plane. The *substantia nigra* and the greater part of Forel's area did not appear macroscopically altered. In specimens treated by Marchi's method degenerated fibres were seen in the regions of the lenticular ansa, capsule of red nucleus, and lenticular nucleus, some of them reaching the putamen. The author points out that his observation agrees with the views recently expressed by C. and O. Vogt on the genesis of choreo-athetotic movements. C. d. F.

Fuchs, A. Experimentelle Enzephalitis. [**Experimental encephalitis.**] *Wien. med. Wchnschr.*, 1921, **71**, 710.

Some years ago the author showed, at a meeting of the Wiener Verein für Psychiatrie und Neurologie, some cats in which a choreiform syndrome had been caused by means of an injection of a 0·1 per cent. solution of guanidine. The peculiar symptomatology began after a period of latency, with frequent sneezing and a slight conjunctivitis, after which the involuntary movements made their appearance. They were accompanied by clonic convulsions which rapidly became more intense and frequent. The final symptoms consisted in paresis of the hind limbs and urinary bladder followed by death. At the autopsy of the poisoned animals pneumonia was found, and in the central nervous system, besides intense congestion, a great number of minute haemorrhages diffusely spread over the white and grey matter of the brain and spinal cord. The author had chosen guanidine for his experiments because this substance appears to form spontaneously in the body under the influence of various infectious agents. Soon afterwards v. Economo published his first observations on lethargic encephalitis and the author restarted his experimental investigations with the object of finding out if, by the use of smaller doses of guanidine, a true encephalitic process could be caused in cats or other laboratory animals. He now reports that this proved to be the case and that, by means of guanidine, meningo-encephalitic lesions are obtainable in cats which do not

differ from those of lethargic encephalitis. He found, in addition, that a similar pathological condition can be brought about in dogs by first performing an Eck's fistula (anastomosis between vena cava and portal vein) and then feeding the animals with meat. The consequences of such an experiment have long been known to physiologists, but, as far as Fuchs was able to ascertain, no one appears to have taken the trouble to investigate the central nervous system histologically where an encephalitic process could be observed.

Unluckily, Fuchs does not give any histological description of these various forms of experimental encephalitis, which would have been particularly interesting in connexion with the pathology of lethargic encephalitis. He says that the material obtained from his experiments was handed over to Pollack for investigation in Marburg's laboratory, but nothing precise is said as to the results of the investigation, and it is doubtful if they were ever published. The only important reference made by Fuchs in this connexion concerns a paper by Rosenthal, who, at about the same time as and independently of Fuchs, also used guanidine for his experimental researches on the amoeboid transformation of neuroglia cells (*Histol. u. histopath. Arb. über d. Grosshirnrinde*, 1912, **6**, 89). Rosenthal used rabbits for his experiments and as a matter of fact speaks of guanidine-encephalitis, but the description he gives of it and the pictures illustrating his paper do not appear to justify the use of the term encephalitis. Indeed, poisoning with guanidine, when sufficiently protracted, causes various, possibly degenerative, alterations of nerve-cells and an intense reaction, on the part of the neuroglia, but no inflammatory changes such as one may see in cases of lethargic encephalitis or as described in animals experimentally infected with an encephalitic virus. C. d. F.

Micheli, F. Intorno all' etiologia dell' encefalite epidemica. [**On the aetiology of epidemic encephalitis.**] *Riforma med.*, 1921, **37**, 9.

Micheli's paper is only a review of recent investigations on the aetiology of lethargic encephalitis. It is, however, important because it gives further details as to the micro-organism isolated in his Institute by Bastai (see *Medical Science*, 1920–21, **3**, 560, and this number pp. 412, 413). This micro-organism appears as a very small coccus, of roundish or oval shape, and measures from 0·3 to 0·5 μ. Sometimes it occurs in still smaller, not measurable dimensions. Its arrangement may vary; it is Gram-negative; it stains particularly well with Giemsa's fluid. At first it grew only in ascitic fluid and Noguchi's tissue medium, taking from five days to one month to develop. Subcultures were more easily obtained and now the micro-organism grows at 37° C. in ordinary media, in which it forms very minute and transparent colonies. It is not haemolytic; it does not produce any green pigment in media containing blood; it is not dissolved by bile; it does not coagulate milk. It ferments glucose, levulose, and inulin. When cultivated in ascitic fluid it passes through the filters Berkefeld N and and Chamberland A 3. It is pathogenic for the dog, cat, rabbit, guinea-pig, and rat, particularly when transmitted from animal to animal by intracerebral inoculations. It can be easily recultivated from animals infected with brain emulsions, and, with difficulty, also from those inoculated with filtered cultures. The virus can be kept in 50 per cent. glycerol for months.

In the same paper Micheli briefly refers to another similar virus cultivated by Maggiore and Sindoni (*Pediatria*, 1920, **28**, 985) from the blood and cerebrospinal fluid of some cases of lethargic encephalitis. These authors have also been able to isolate, by means of Tarozzi's and Noguchi's culture media, a small anaerobic, Gram-negative coccus, which is stainable by Leishman's fluid. When inoculated into rabbits it gives origin to a meningo-encephalitis characterized by perivascular haemorrhages and polyblastic infiltrations particularly noticeable around small veins. According to Micheli the minute coccus of Maggiore and Sindoni does not appear to be essentially different from Bastai's micro-organism; however, these authors are not of the same opinion, and think that their coccus has the same cultural characteristics as Flexner and Noguchi's globoid body. They have, therefore, put forward the suggestion that lethargic encephalitis and Heine-Medin disease may be only different manifestations of an essentially identical virus. C. d. F.

Meleny, H. E. Degeneration granules in brain-cells in epidemic encephalitis. *Arch. Neurol. & Psych.*, 1921, **5**, 147.

In the routine examination of sections from the brain of a case of epidemic encephalitis, minute granules were observed by Meleny in degenerated nerve-cells from areas affected by the disease. These granules are best shown in pieces of tissue fixed in Zenker's or Helly's fluid, embedded in paraffin and stained with eosin-methylene blue or by Bensley's modification of Altmann's method. To demonstrate them with eosin the author recommends a mixture of equal parts of strong alcoholic and 5 per cent. watery eosin solutions staining 45 minutes at 56° C. Demonstrated by these stains the granules appear as minute spherical masses, measuring from 0·5 to 2 μ in diameter, sharply outlined and highly refractile. The largest ones are nearly half as large as the nucleoli found in the same nerve-cells and often have a minute colourless centre as though the stain had not thoroughly penetrated. They also are frequently surrounded by a clear zone in the cell cytoplasm. Their number appears to have no relation to the degree of degeneration of the nerve-cell. Frequently only a single granule is found in a cell, while other cells, the appearance of which is no more abnormal, contain forty or fifty granules. The degenerated cells are found only in areas in which there are other lesions characteristic of the disease. In the case of epidemic encephalitis investigated, the granules were found in the occipital cortex, the basal ganglia, the pons, and the medulla. In the spinal ganglion cells of the same case granules were found which gave the same staining reactions but were more irregular in outline, more numerous, and usually arranged in small rosettes. Sections from the central nervous system treated for 5 minutes with 10 or 20 per cent. nitric acid showed the granules as brilliantly as before, whereas sections similarly treated with 5 per cent. NaOH showed them hazily outlined and dull red in colour. The granules are not specific of epidemic encephalitis as shown by their occurrence in the same situations in four cases of poliomyelitis, and in one of tuberculous meningitis associated with lymphocytic infiltration of the brain-stem. But they were not seen in cases which did not show an involvement of the central nervous system. According to Meleny the granules should therefore be considered as 'some form of cytoplasmic degeneration'. C. d. F.

Globus, J. H., and **Strauss, I.** **Subacute epidemic encephalitis.** *Arch. Neurol. & Psych.*, 1922, **7**, 267.

The clinical history and anatomical findings of a case described by the authors at the 47th annual meeting of the American Neurological Association are an important departure from the observations made in the acute form of epidemic encephalitis. The patient, a man 53 years of age, had begun to complain of occasional headache and vertigo six months before admission to hospital. Physical examination revealed paresis of the lower extremities, especially on the left side, difficulty in gaining and maintaining the sitting posture, and a Babinski plantar response on the right side. In addition, there was on the right side paresis of the internal rectus; on the left side complete paralysis of the external and internal recti and incomplete paralysis of the superior and inferior recti and superior oblique. Cerebrospinal fluid was under increased pressure, with a faint trace of globulin and albumin. Wassermann test negative. After a period of improvement lasting five weeks, a sudden decline was accompanied by increased ptosis of the eyelids, further limitation of the eye movements, diminution of muscular power, and impairment of speech. During the next eight days the patient's condition became progressively worse and death supervened with symptoms of bulbar paralysis. The necropsy showed extreme congestion of the leptomeninges most pronounced on the ventral surface of the medulla and pons. On microscopic examination of the brain, lesions characteristic of the acute form of epidemic encephalitis, such as small-celled perivascular infiltrations, were found only on close scrutiny in the neighbourhood of the Sylvian aqueduct and region of inferior olives. The most important lesions consisted of: adventitial thickening leading to marked fibrosis of the outer wall of the blood-vessels; intimal thickening from swelling and re-duplication of the endothelium of the smaller vessels; formation of small capillaries; accumulation of lipoid substances in the adventitia of large blood-vessels; focal aggregations of neuroglia cells; accumulation of large glia cells about smaller vessels; extravascular haemorrhages, 'indicating the terminal and destructive action of the virus on vessel-wall'. No true atherosclerotic changes were seen. From these findings and from the observations made in six cases of the acute form of lethargic encephalitis, the authors came to the conclusion that 'the primary attack of the virus is on the wall of the small- and medium-sized vessels and that the vessel-wall is affected by the virus in a manner proportionate to its virulence'. When the virus reaches the blood-vessels in a small amount or in an attenuated form, lesions indicating subacute and proliferative lesions follow, as shown in the present case and as happens in certain mineral poisons exemplified by lead encephalitis. The authors therefore suggest the grouping of epidemic encephalitis into: an acute infiltrative form with the predominant feature of perivascular infiltrations; an acute haemorrhagic form; a subacute 'productive' form as described in this paper. Both the fatal haemorrhagic type and the mild productive form may be one of the outcomes of the acute infiltrative form.

C. d. F.

Watson, G. A. A case of encephalitis lethargica involving chiefly the cerebral cortex. *Neurol. & Psychopath.*, 1920, **1**, 1. (*Arch. Neurol. & Psych.*, 1921, **6**, 214.)

The patient, a woman aged 28, presented at first a picture of agitated melancholia and remained in this condition without change for four months. Then for three days she seemed to be very ill and vomited several times. During the ensuing two months she improved mentally, but began to complain of pain in the back and down the left thigh, and she limped when walking. This condition continued for another two months, when she lost her power of speech and the right side of the tongue became paralysed. She was drowsy and lethargic. Eleven days later complete right hemiplegia with anaesthesia and analgesia was observed. Optic neuritis of moderate degree was present. A week later the hemiplegic limbs showed a marked muscular atrophy and she died the following day. During her illness her temperature was subnormal and the blood count showed a definite leucocytosis. At the post-mortem examination a large area of recent softening with adherent membranes was found in the left hemisphere. After hardening, sectioning of the area disclosed streaks of vascular congestion which were not readily apparent in the rest of the brain, but no large haemorrhages. Microscopically, the meninges showed increase of blood-vessels with marked congestion and small haemorrhages. In the area of softening there was a very conspicuous increase of vessels with cellular proliferation mainly round the vessels, but in the most affected parts spreading widely into the surrounding tissue. 'The proliferative elements were lymphocytoid, plasma and pseudoplasma cells, but mainly polyblasts, epithelioid and reticulate types of cells, obviously originating from the adventitia.' Neuroglia cells were somewhat increased and the endothelium of the vessels showed proliferation. Small haemorrhages were found around the vessels, though they were not numerous except in the putamen and left precentral convolution, where they were rather large. Many veins showed partial occlusion by thrombi. Rarefied sieve-like spaces were noticed, especially in the white matter, containing amorphous deposits and proliferated cells. Nerve-cells were affected in the softened area corresponding to the patchy intensity of softening. The precentral and subfrontal regions, the insula and part of the temporal lobe were mostly involved. The putamen seemed to have been most affected while the remaining portions of the basal ganglia were little involved. In the temporal region the process appeared to be of longer standing and not as acute. Changes similar in character but much less intense in degree were observed in other parts of the brain, in the pons, spinal cord, and medulla, where round cell infiltrations were most marked. The nerve-roots and spinal ganglia also showed congestion, cellular proliferations ,and small haemorrhages. The condition is termed a meningo-encephalo-myelitis on account of its widespread distribution. However, one feels somewhat doubtful whether cases of the sort are due to the same aetiological factor as the ordinary types of lethargic encephalitis.

C. d. F.

BACTERIOLOGY

Fasiani, G. M. Ricerche batteriologiche sulla gangrena gasosa. [**Bacteriological investigations on gas gangrene.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 135.

Very accurate investigations were carried out on 34 cases of gas gangrene with the following results: the microbic flora is varied and complex, but anaerobic germs constantly occur in changing number and of different kind. Thus there are cases connected with one anaerobic species only, and others due to the association of various anaerobic germs. However, these bacteriological differences do not impart to the individual cases any special clinical or pathological features. Among the anaerobic germs cultivated from cases of gas gangrene well-defined species can be recognized, and no fact was observed in support of the opinion expressed by other authors as to the possible transformation of one anaerobic form into another. Anaerobic germs of gas gangrene may be subdivided into three groups: (1) Non-motile butyric bacilli. (2) Motile butyric bacilli. (3) Putrefying bacilli. Among those of Group I various strains occur all belonging to one species, generally spoken of as *B. perfringens*. They are characterized by absence of motility, with only occasional sporulation, remarkable fermentation of carbohydrates and very slight of proteins, pathogenic properties manifesting themselves as progressive and fatal infections with sero-haemorrhagic oedema and collections of gas. The differences between the various strains of Group I concern the form, the sporulation, the type of colonies, the proteolytic and pathogenic properties. The serum of animals treated for a sufficiently long time with cultures from bacilli of Group I has a specific antipathogenic and antitoxic activity. Among the strains belonging to Group II, the author has found two non-pathogenic and two pathogenic species. Of these last, one is identical with B. of Ghon and Sachs (*Vibrion septique* of Pasteur); the other is similar to B. of Novy, and up to a point to *B. oedematiens*, *B. bellonensis*, *B. der Gasoedem.* B. of Ghon and Sachs is motile, precociously and abundantly spore-bearing with many swollen forms. It is filamentous when growing in the peritoneal cavity, and sometimes in cultures; it actively ferments carbohydrates and has a weak proteolytic action; it does not produce sulphuretted hydrogen or indol; when inoculated into guinea-pigs or rabbits it causes fatal infections with haemorrhagic oedema, but without liquefaction of muscular tissue; it is specifically agglutinated and neutralized by immune sera. B. of Novy is less motile, and less actively spore-producing; it does not grow into filaments and produces sulphuretted hydrogen and indol; the other characteristics are similar to those of B. of Ghon and Sachs. The two non-pathogenic species of the second group correspond respectively to *B. fallax* of Weinberg and Séguin (species 6 and 7 of von Hibler, B. of Stolz) and to *B. tertius* of Henry (species 9 of von Hibler). Both species are formed of motile and thin bacilli which actively ferment carbohydrates but are not proteolytic. *B. fallax* rarely bears spores, while *B. tertius* is characterized by a large oval spore. Among the strains of Group III the author has identified *B. sporogenes* of Metschnikoff and *B. putrificus* of Bienstock. Both of them cause a putrid decomposition of proteins, but the former is large with a central or subterminal oval spore, while the latter is thin with a distinctly

terminal spore. Forms similar to these two frequently occurred in the cases examined by the author, but could not be completely identified. From the whole investigation it appears that the species which most frequently, and perhaps essentially, cause gas gangrene in man are *B. perfringens*, B. of Ghon and Sachs, B. of Novy. C. d. F.

Ciarla, E. Su nuove forme spirochetiche riscontrate nei feti eredosifilitici. [**On new spirochaetal forms found in heredo-syphilitic foetuses.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 81.

Investigations were carried out by means of the following method: Small pieces of fresh tissues are fixed and mordanted for 8 days in a mixture filtered before using, and consisting of distilled water 500 c.cm., potassium bichromate 10 gm., chromium fluoride 10 gm., chromalum 20 gm., copper acetate 5 gm., acetic acid 5 c.cm. The pieces are then passed for 12 days into a second mixture consisting of distilled water 100 c.cm., potassium bichromate 2 gm., chromium fluoride 2 gm., chromalum 4 gm., osmic acid 0·25–0·50 gm. to be added last and after having filtered the mixture. There should be about 20 c.cm. of mixture to every piece, and the bottle should be moved about every day, adding some fresh fluid when the odour of osmic acid is no longer noticed. After washing for 24 hours in running tap-water, the pieces are embedded in celloidin in the usual way. Sections are cleared with carbol xylol and mounted in balsam. A previous counter-staining is possible, but not necessary. In successful specimens spirochaetes stand out stained greyish-black on a yellowish background, if no counter-staining was carried out.

The method was systematically applied to the study of various tissues from 10 heredo-syphilitic foetuses, and from a great quantity of control material comprising still-born but not syphilitic foetuses, embryos from various animals, testes from rabbits experimentally infected with syphilis, tissues from cases of G.P.I., tabes dorsalis, syphilitic aortitis, &c. The results obtained are illustrated by three beautiful plates, and summarized in the following conclusions: (1) The osmio-bichromic impregnation is sufficient to show spirochaetic forms. (2) In heredo-syphilitic foetuses, spiral micro-organisms occur with the characteristics of the genus *Treponema* and *Spirochaeta*. Of these some are similar to *Spirochaeta pallida*, many are morphologically different from this last. (3) The spirochaetic forms newly observed are characterized by the presence of an axial cylinder (screw-like forms), by a terminal efflorescence of changing shape, and by varying dimensions which may be smaller, the same or greater than those of *Spirochaeta pallida*. In addition, rare rosette-like forms are noticeable in heredo-syphilitic foetuses. (4) None of the new forms appear to exist in other materials, whether syphilitic or not. (5) The new forms probably belong to the biological cycle, of *Spirochaeta pallida*, and are, perhaps, produced under particular life conditions not as yet clearly ascertained. C. d. F.

Hayashi, N., and **Kibata, T.** **Spirochaetal organisms in the tissues in acute yellow atrophy of the liver.** *J. Infect. Dis.*, 1922, **30**, 64.

The authors record briefly the discovery of a spirochaete in the liver and certain other organs from a typical case of acute yellow atrophy, fatal in one week. The autopsy was made only two hours after death. Inoculation and cultures of post-mortem material were made by Noguchi, but failed

to reveal the presence of *Leptospira ictero-haemorrhagica* in the case. In the intestine there were groups of thread-like organisms measuring 10–12 microns, while in the liver, in addition to similar but shorter rods, there were numerous minute bodies 'of diplococcoid or diphtheroid type' intra- and inter-cellular. The necrotic epithelium of the tubules showed a typical spiral organism in addition to the rods and coccoid bodies. The rod-shaped bodies and spirals were stained by Levaditi's method. In one place it is stated that the 'coccoid body was not demonstrated by the Levaditi method' while in another it is said that the coccoid body is not a bacterium 'from the positive Levaditi reaction'. An error has also crept into the numbering of the figures.

Cases of acute haemorrhagic jaundice were also examined, and in 3 out of 6 the three types of bodies above mentioned were found. No such organisms were found in normal human intestines (5 cases), in normal guinea-pigs (10 cases), or in the intestine of a man with an undetermined type of spirochaetal infection. While the aetiological relation of the micro-organism to acute yellow atrophy cannot be determined yet, the parallelism existing between the abundance of the organism and severity of the lesion suggests to the authors the probability of such a relation. W. B.

Noguchi, H. A note on the venereal spirochaetosis of rabbits. *J. Am. M. Ass.*, 1921, **77**, 2052–3.

Noguchi describes a form of venereal spirochaetosis occurring spontaneously in rabbits, caused by a spirochaete, *Treponema cuniculi*, and somewhat resembling the experimental syphilis of rabbits. The lesions consist of scaly papules on the genital region, and the affection may be transmitted directly by mating or indirectly by applying the exudation with or without scarification. *T. cuniculi* is rather longer and coarser than the *T. pallidum* and more rapid in its movements of rotation. The incubation period varies from 20 to 88 days. Inoculation of apes and the Wassermann reaction were both negative, but the spirochaetes disappeared from the lesions in 24 hours after an injection of arsphenamine. Noguchi finds the following strain useful for demonstrating both *T. cuniculi* and *T. pallidum*.

Fix films for 5 minutes in 1 part formaldehyde, 9 phosphate solution (88 parts Na_2HPO_4, 12 parts KH_2PO_4). Flood with saturated alcoholic solution of gentian violet or fuchsin; wash and dry. C. F. M.

Klarenbeek, A. Ueber das spontane Vorkommen der dem Syphilisparasiten ähnlichen Spirochäte beim Kaninchen (*Treponema pallidum* var. *cuniculi*). [**On the spontaneous occurrence in rabbits of spirochaetes similar to the parasites of syphilis (*Treponema pallidum* var. *cuniculi*).** *Centralbl. f. Bakteriol.* (&c.), Abt. 1, 1921, Orig. **87**, 203.

From his observations the author considers that the *Treponema* found in spontaneous lesions in rabbits is indistinguishable from *T. pallidum*. In experimental infections there are only very slight and inconstant differences between them, so that he is inclined to regard the rabbit treponema as a variety of *T. pallidum*, and he proposes the name *T. pallidum* var. *cuniculi* and the disease lues cuniculi. W. B.

Roaf, H. E. The Wassermann reaction in relapsing fever. *Brit. J. Exper. Pathol.*, 1922, **3**, 59.

It appears probable that a transient positive Wassermann reaction may be found to be a constant phenomenon during the acute stage of relapsing fever. The transient character distinguishes it from the reactions due to syphilis. If the positive result is observed on every occasion in a particular patient, it may be suspected that he has syphilis also. P. F.

Jeanselme, E., et **Pomaret, M.** Étude expérimentale des ' phénomènes de choc ' produits par les arsènes et les novarsénobenzènes. [**Experimental study on shock phenomena produced by arsenobenzol and novarsenobenzol compounds.**] *Ann. de méd.*, 1921, **10**, 467.

The authors put forward the thesis that the immediate toxicity of ' 606 ' and ' 914 ' compounds, when injected intravenously, is due to the phenolic groups exerting a flocculating action on the plasma proteins when the conditions are sufficiently acid. The addition of 1 gm. of ' 914 ', dissolved in as little water as possible, to 100 c.cm. of freshly prepared serum, produces a turbidity which after 24 hours becomes a precipitate. This is soluble in sodium carbonate. They show that in a dog under chloralose, the intravenous injection of non-toxic doses of ' 914 ', when they are dissolved in 2 per cent. citric acid, will cause a fall in blood-pressure of 100 mm. The same doses injected in neutral solution produce no fall in blood-pressure. The fall in blood-pressure produced by the acid solution may be countered by the injection of $NaHCO_3$, but this salt is powerless against the shock and fall of blood produced by injecting ' 606 ' in acid solution. The fall in blood-pressure produced by the injection of ' 606 ' or ' 914 ' in acid solution is in both cases averted by the previous injection of 0·5 mgm. adrenalin.

That the shock effects following immediately in some cases after injection of ' 606 ' and ' 914 ' are not due to the presence of the 'arsenoxide' is shown by the fact that the arsenoxide itself causes a rise of blood-pressure when 10 c.cm. of a 1 per cent. solution are injected intravenously into the dog under chloroform. J. H. B.

Wadsworth, A. B., and **Hoppe, E. N. The action of bacterial culture products on phagocytosis.** *J. Immunol.*, 1921, **6**, 399.

In this study the leucocytes of the dog were used, their phagocytic powers being determined against staphylococci sensitized by horse serum. The tests were carried out *in vitro*, the leucocytes being subjected to the action of diphtheria toxin and 15 other toxins and culture broths of widely differing bacterial species. In every case the phagocytic power of the leucocytes was inhibited in a high degree. Tests carried out chiefly with diphtheria toxin showed that its inhibiting action was immediate, and could not be prevented by antitoxin nor be destroyed by heat even at 120° C. for an hour. Exposure of the toxins of *B. diphtheriae* or *B. tetani* to trypsin or pepsin exerted a destructive effect on the inhibiting power of the toxin. Variation in the composition of culture broths, although greatly influencing the toxin titre, produced no marked effect on the inhibiting power.

W. B.

Jervell, F. The influence of temperature upon the agglutination of the red blood corpuscles. *J. Immunol.*, 1921, **6**, 445.

Because haemolysis occurs more quickly at 37° C. than at a lower temperature it has been supposed that the same is true of agglutination of red blood corpuscles. Experiments made by the author show, however, that a more pronounced agglutination and a greater absorption of agglutinin take place at a low (8° C.) than at a high temperature (37° C.). Indeed, agglutinin absorbed at a low temperature (8° C.) may be partly given up when the corpuscles are placed at a temperature above 25° C. W. B.

Kobayashi, R. On the serum treatment of tetanus, in special reference to the point of attack and the path of spread of tetanus toxin in the animal body. *Kitasato Arch. of Exper. Med.*, 1921, **4**, 217–80.

This is an elaborate research into the still disputed path of spread by which tetanus toxin progresses from a wound towards the central nervous system. By path of spread the author means the route by which tetanus toxin is transmitted from the point of entrance to the other parts of the body finally to reach the point of attack. The author has carried out a large number of experiments, the results of which he clearly sets forth in a series of tables, which lead him to the conclusion that in the animal, as well as in the human body tetanus toxin is absorbed from the foci into the lymphatic spaces of the peripheral nerves. That portion of the absorbed toxin which enters the endoneural lymphatic spaces attacks the peripheral nerve-fibres, while the remaining portion is transmitted still farther centrally and attacks the spinal motor-cells. Thus the point of attack of tetanus toxin is the whole of the neurons of the peripheral motor-nerves. Anti-tetanic serum having a high antitoxin content is a rational remedy in tetanus, and in the opinion of the author it should be introduced into the subarachnoid space as soon as possible and in as large a dose as possible in order to secure the best results. W. B.

Capone, G. Sul meccanismo d'azione dei cosidetti liquidi aggressici. [**On the mechanism of action of the so-called aggressin fluids.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 17.

Conclusions: Bacterial extracts from broth cultures have, *in vitro*, an antibacteriolytic action similar to that of exudation fluids obtained from infected animals. Natural or artificial aggressins prevent bacteriolysis *in vitro* by altering the complement. Aggressins have no apparent action on bacteriotropic sera, and hinder or reduce to a minimum the phagocytic activity of leucocytes stimulated by bacteriotropins. C. d. F.

Carbone, D., Ramazzotti, G., Mazzucchi, M., e Monti, P. C. Le reazioni sierodiagnostiche dei microorganismi banali. 1° L'agglutinazione nel gruppo dei mesenterici. [**The sero-diagnostic reactions of common bacteria. 1. Agglutination in the group of *B. mesentericus*.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 29.

Carbone, D., e Venturelli, G. 2° L'agglutinazione nel gruppo del *B. asterosporus*. [**2. Agglutination in the group of *B. asterosporus*.**] Ibid., 1921, **2**, 191.

(1) Different strains of the same species agglutinate one another at a very high titre as far as regards *B. aterrimus* and *B. carotarum*. The

same does not happen in the case of different strains of *B. lactis niger*. All bacteria of the group of *B. mesentericus* are interrelated; a special subgroup is formed of *B. aterrimus*, *B. mesentericus fuscus*, *B. carotarum*, *B. tyrosinogenes*. *B. teres* is probably different from *B. tyrothrix filiformis*, and *B. lactis niger* from *B. aterrimus*. This last is culturally connected with *B. mesentericus niger* of Karl. Normal rabbits' serum, even at a dilution of 1:50, has no agglutinating power on any of the microorganisms of the group investigated. *B. aterrimus*, *B. mesentericus fuscus*, and *B. lactis niger* are sometimes pathogenic for the rabbit.

(2) The group of *B. asterosporus* cannot be subdivided into distinct species on the basis of agglutination reactions. As in the case of the groups of *B. coli communis*, *B. fluorescens*, and *B. lactis niger*, agglutination is specific for the strains but not for the species. C. d. F.

Bufalini, M. Influenza della splenectomia sulla distruzione dei batteri nell'organismo. [**Influence of splenectomy on the destruction of bacteria in the organism.**] *Sperimentale: Arch. di biol.*, 1921, **75**, 437.

Experiments were made in rabbits by means of pure cultures of *B. typhosus* and *Staphylococcus pyogenes aureus*. The results obtained are: In intact animals the elimination of bacteria through the liver and bile begins about 9 hours after their intravenous inoculation and reaches a maximum at about the 48th hour, at which time the number of colonies obtainable in agar plates inoculated with 10 drops of bile from an infected animal is such that they cannot be counted. After splenectomy the number of colonies obtainable in the same experimental conditions is considerably smaller than in the case of intact animals. The same can be said in regard to the blood, the inoculated bacteria disappearing much sooner from the circulation in the case of animals deprived of the spleen than in the case of intact ones. A partial, but, according to the author, not quite satisfactory, explanation of these results was found in the fact that after splenectomy a very rapid and intense phagocytosis of the injected bacteria takes place. C. d. F.

Osato, M. Beiträge zum Studium der Lymphe. I. Vergleichende Untersuchung vom Antikörpergehalt des Blutes und der Lymphe und seine Beeinflussung durch verschiedene Lymphagogaarten. [**Contributions to the study of the lymph. Comparative study of the antibody content of the blood and lymph and the influence of different lymphogogues.**] *Tohoku J. Exper. M.*, 1921, **2**, 325.

The author actively immunized dogs with typhoid bacilli or with sheep erythrocytes, and, having examined the agglutinin or haemolytic titre of the blood serum and the lymph as the latter issued from the thoracic duct, he found that, although the titre of both antibodies in the lymph was less than it was in the blood, they could be augmented by the injection of lymphogogues of the first class. There was a diminution of titre with lymphogogues of the second class. The fluctuations corresponded on the whole with the change in the weight of dry substance and total nitrogen of the lymph serum. W. B.

Dominici, A. Influenza delle proteine sulla fagocitosi studiata *in vitro*. [**Influence of proteins on phagocytosis investigated *in vitro*.**] *Riforma med.*, 1921, **37**, 800.

The present paper is related to recent investigations on the effects of intravenous inoculations of heterogeneous proteins, to which reference has already been made (see Pentimalli, *Medical Science*, 1922, **5**, 522). The author has studied the influence of such inoculations on phagocytosis investigated *in vitro*, *B. typhosus* being used as a test. The conclusions reached are: heterogeneous proteins put in contact with typhoid bacilli in guinea-pigs' blood influence phagocytosis in a different way according to the doses of protein. Small doses markedly favour phagocytosis, while large ones diminish or prevent it. These effects appear due to products from the fission of the proteins under the influence of blood ferments. Such products impart to polymorphocytes a strong chemotropic power which is positive or negative according to the amount of products from fission present in the blood. This appears to prove the supposition that phagocytosis plays an important rôle in the therapeutic results obtainable in infections treated by means of protein vaccination. C. d. F.

Morgenroth, J., u. Abraham, L. Depressionsimmunität bei intravenöser Superinfektion mit Streptokokken. [**Depression immunity with intravenous superinfection of streptococci.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 163.

It was recently (1920) shown by Morgenroth and his co-workers that mice affected with a chronic streptococcic infection show an immunity ('depression immunity') when a superinfection is induced by virulent streptococcic cultures. This depression immunity may show itself in the fact that the animals react to a lethal dose of streptococci with a chronic infection instead of with an acute sepsis. In the original investigations the superinfections were brought about by subcutaneous inoculations. In the present paper the authors detail experiments in which mice were previously infected with cultures of streptococci administered subcutaneously, intraperitoneally, or intravenously, being subsequently superinfected within 1–3 days with virulent streptococci introduced intravenously. An immunity was noted manifesting itself either in the prolongation of life or absence of a fatal issue altogether, although the controls died of acute sepsis. W. B.

Lange, B. Untersuchungen über Superinfektion. [**Researches on superinfection.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 135.

Studying the problem of 'depression immunity' (Morgenroth, *vide supra*) in superinfections the author shows it is not apparently universal, or, at any rate, it varies in degree. In guinea-pigs infected with the bacillus of fowl cholera, or in mice infected with the bacillus of mouse typhoid or *B. gärtneri* it is very slight. A much higher degree of immunity was found in rabbits infected with streptococci and pneumococci. W. B.

Munter, H. Über Abspaltung bacteriolytischer und hämolytischer Amboceptoren. [**On the splitting off of bacteriolytic and haemolytic amboceptors.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 152.

After allowing bacteriolysins to interact with the homologous bacterial cultures the author shows that the union may be split so that it is possible

to demonstrate afresh a lytic action *in vitro* or *in vivo* (Pfeiffer's phenomenon). In a second series of experiments the same facts were shown in the case of haemolytic amboceptors, as was first proved by Morgenroth (1903). Contrary to the latter the present author shows that the separation of haemolytic amboceptor may be brought about without the presence of uncharged red blood corpuscles. W. B.

Cutler, E. The relation of the hypophysis to antibody production. *J. Exper. M.*, 1922, **35**, 243.

After partial removal of the hypophysis cerebri, guinea-pigs were immunized with *B. typhosus* and were found to behave like the normal controls which had not been subjected to the operation. When previously immunized partial hypophysectomy had no influence on the continued production and persistence of typhoid agglutinins, haemagglutinins, or haemolysins. Feeding with hypophysis was also without influence. Total removal of the hypophysis proved fatal in 24 to 48 hours. W. B.

Schmidt, P., u. **Happe, H.** Weitere experimentelle Studien zur Anaphylaxiefrage. [**Further experimental studies on the anaphylaxis question.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 253.

In 1913 Bordet showed that anaphylactic shock can be induced by serum which has been in contact with agar. Among others, Friedberger alleged that this might be due to the fact that agar is impure and contains protein. The present authors show that anaphylaxis can be induced when serum has been in contact with agar deprived of all its protein by Klostermann's method (*Ztschr. f. Hyg. u. Infektionskrankh*, 1921, **94**, 262). Inactive serum or physiological salt solution in contact with protein-free agar has no effect. The agar remaining after contact with serum is also harmless. Berkefeld filtration makes agar anaphylatoxin inert. The nature of anaphylactic shock is also dealt with. W. B.

Corper, H. J., Black, Louisa T., and **Moore, Mary. The effect of the Röntgen ray and mustard gas (dichlorethylsulphide) on active anaphylaxis in the guinea-pig.**] *J. Infect. Dis.*, 1921, **30**, 50.

In guinea-pigs a maximum non-lethal dose of Röntgen rays given seven days before or coincident with the sensitizing injection of egg-white or normal horse-serum or seven days before or with the second injection causes no appreciable ameliorating influence on the reaction resulting from the second injection of these proteins. A slight increase in the severity of the reaction was noted in guinea-pigs receiving the exciting injection of protein when Röntgen rays had exerted a profound influence on the blood-forming mechanism, as indicated by the leucocytic count. Subcutaneous injections of dichlorethylsulphide were without appreciable effect on anaphylaxis. W. B.

Oshikawa, K. Beziehungen zwischen Antigen und Antikörperbildung. (Der Einfluss des parenteralen Antigendepots auf die Antikörperbildung.) [**Relationship of antigen and antibody formation. (The influence of parenteral antigenic depôts on antibody formation.)**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **33**, 306.

The author refers to the theories which have been held to explain the formation of antibodies, and deals in some detail with the most recent one,

viz. that of Sahli (1920), according to which all antibodies are supposed to pre-exist in the blood and tissue fluid. When antigen is introduced it combines with the pre-existing antibody, which is replaced in excess by the antibody secretion from the cells. If this is correct the prolonged sojourn of antigen in the body should materially influence antibody production, as the lowering of the normal antibody level by progressive absorption of antigen would lead to a greater and greater antibody production. The present author shows that this is not the case. His method was to introduce small quantities (0·5 of a loopful) of a killed passage culture of *Proteus* X 19 into the tip of the ear and to remove the whole ear at the base, one hour later. All the animals show considerable or even marked agglutinin in the serum. In a second series of experiments the dose of antigen was reduced to 0·01 of a loopful and the injection was made intracutaneously in the tip of the ear, after which the whole ear was amputated. Even when the amputation was carried out 10 minutes after the injection of antigen the agglutinogenic response was marked, the agglutinin titre rising to 1 : 1,200. A longer sojourn of the antigen depôt in the body was not only of no advantage but apparently deleterious. W. B.

Oshikawa, K. Antikörperbildung durch Transplantate. [**Antibody formation by grafting.**] *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1921, Orig. **33**, 297.

In 1911 Friedberger and Girgolaff showed that the transplantation of certain organs from immunized animals into normal animals of the same species led to the appearance in the latter of antibodies which were specific for the antigens with which the first animals had been inoculated. Apart from haemopoietic tissues, kidney was found to be suitable for such experiments. The present author, working under Friedberger's direction, has extended this line of research to transplantation of skin. Rabbits were inoculated subcutaneously with cultures of *B. paratyphosus* B or with emulsions of sheep erythrocytes, and when specific agglutinins and lysins had appeared in their sera, skin grafts were taken from the ear and implanted on a specially prepared area of the ears of normal rabbits, the sera of which was subsequently tested. During the time that the recipient was being prepared the graft was kept in saline solution. In general, three grafts were taken from each ear of the immunized animal. The sera of the recipients showed in all cases a development of specific antibodies which was all the more marked when the healing of the grafts was perfect. In one set of experiments it was shown that skin grafts of normal rabbits could be treated with antirabbit immune serum and complement without detriment to the healing process. W. B.

Hooker, S. B., and **Anderson, Lillian M.** **The specific antigenic properties of the four groups of human erythrocytes.** *J. Immunol.*, 1921, **6**, 419.

In the author's experiments it was found that the sera of normal rabbits possess weak agglutinins for the four groups of human red blood corpuscles. In the case of certain rabbits this agglutinative power is group specific, being especially marked in the case of the cells of Groups II and IV. Each of the four types of human sera contains agglutinins for rabbits'

erythrocytes, but there is no group specificity. Human isoagglutinin 'b' present in Groups I and II sera is specifically absorbed by the erythrocytes of the rabbit. Group specific haemagglutinins demonstrable by absorption were produced by injection of rabbits with type cells. Group I cells, at least those of certain individuals, were found to contain a specific agglutinogenic component that does not exist in the other group cells examined. Group specific haemolysins and complement-fixing antibodies are developed with the agglutinins. Many rabbits failed to produce group-specific antibodies, although no cause for this variation was discovered by the authors.

W. B.

Ottenberg, R. Hereditary blood qualities. Medico-legal application of human blood grouping. *J. Immunol.*, 1921, **6**, 363.

This paper is a review of the facts concerning the inheritance of group specific substances in human blood with the object of presenting the possibilities of their practical application and of defining the instances in which they can be used in medico-legal questions. The phenomenon of isoagglutination of red blood cells was first noted by Grünbaum (1900), and by Shattock (1900), but was supposed to be the result of disease. Landsteiner (1901) reduced it to a law and showed that there were three groups. Further, he showed that the phenomenon was due to the presence or absence of two specific agglutinins.

Later, Jansky (1907) showed that there was a small fourth group distinct from the other three groups.

The grouping adopted in the present paper is that of Jansky.

Group.	Serum.	Red Cells.
I.	Agglutinates the cells of the three other groups. Contains agglutinin α and β.	Inagglutinable. Contain no agglutinogen.
II.	Agglutinates cells of Groups III and IV. Contains agglutinin β.	Agglutinated by serum of Groups I and III. Contain agglutinogen A.
III.	Agglutinates cells of Groups II and IV. Contains agglutinin α.	Agglutinated by serum of Groups I and II. Contain agglutinogen B.
IV.	No agglutinative effect. Contains no agglutinin.	Agglutinated by sera of Groups I, II, and III. Contain agglutinogen A and B.

The existence of two specific cell agglutinogens and two corresponding agglutinins have been proved by absorption tests. These two agglutinogens are represented by A and B, and the corresponding agglutinins as α and β.

In 1910 von Dungern and Hirschfeld showed that the agglutinogens A and B never appeared in a child unless present in one of the parents, if present in both parents most of the children inherit it, and if present in only one parent some of the children inherit it.

A as an inherited character, then, is dominant over absent A (Not A) and B is dominant over absent B (Not B), and the two pairs of unit characters A and Not A and B and Not B are inherited independently of each other, and if A or B are present in a child's blood one of the alleged parents must possess it.

Taking, then, the qualities of agglutinability, as those of agglutinating power do not develop until some time after birth, the quality A is dominant to Not A (N A) and B is dominant to Not B (N B). The qualities N A and N B are not simply blanks but definite qualities associated with the

development of agglutinins α and β respectively. The inheritance of A or N A, then, carries three possibilities.

(i) Both parents A gives offspring pure A.

(ii) Both parents N A gives offspring pure N A.

(iii) One parent A and one N A gives offspring hybrid A–N A.

The same three possibilities exist for B or N B. Taking, then, the groups:

Group I can never be hybrid.

Group II can only be hybrid with regard to its dominant quality A, so that there are two types of Group II, pure and hybrid (A–A and A–na, the n a being recessive 'not a' and not apparent but transmissible).

Group III similarly can only be hybrid with regard to its quality B.

Group IV has four possibilities. It may be pure with regard to both dominant qualities A and B, or pure with regard to one while hybrid with regard to the other, or hybrid with regard to both.

These various possibilities are shown graphically in a chart.

The author next considers the possible offspring of unions of a member of one group with another member of the same group, and also the offspring of unions of two different groups. The various possibilities of such unions are shown graphically.

Summarizing these results it is seen that

Unions of I and I give only I.
„ „ I „ II „ „ I and II.
„ „ II „ II „ „ I „ II.
„ „ I „ III „ „ I „ III.
„ „ III „ III „ „ I „ III.
„ „ II „ III may give offspring of any group.

Unions containing a member of Group IV may give offspring of any group. A child belonging to Group I may result from any combination of parents.

From this summary it will be seen in what circumstances it will be possible to say that a given child is not the offspring of an alleged parent.

G. T. W.

Bastai, P. Nuove ricerche intorno ad un virus filtrabile e coltivabile ottenuto in alcuni casi di E.E. [**Fresh investigations on a filter-passing and cultivable virus obtained from some cases of epidemic encephalitis.**] *Boll. d. Ist. Sieroterap. Milanese*, 1921, **2**, 197.

Reference has already been made to previous work of this author on the same subject (*Medical Science*, 1920–21, **3**, 560). He now reports that he has been able to isolate from another case of epidemic encephalitis a virus morphologically, culturally, and biologically similar to that obtained in 1920. The new virus was slightly virulent for monkeys, though one macaque became affected by a malady essentially corresponding to lethargic encephalitis. Rabbits appeared to be much more sensitive and could be infected by intra-testicular, intra-ocular, and intranervous (central and peripheral) inoculations. The intra-ocular inoculations consisted either of injections into the anterior chamber or of simple corneal scarifications. In this last case a keratitis of changing severity was obtained. When this was followed by the death of the animals the virus could be reinoculated from the blood and brain. A fatal infection of rabbits could, in some cases, be brought about also

by skin scarifications, the skin being affected by a herpetiform disease, from which, however, the animals sometimes recovered. The rabbits which had overcome a keratitis were resistant to further inoculations. The author is of the opinion that his virus is, very likely, similar to that obtained by Levaditi, as well as to that of herpes febrilis. C. d. F.

Bastai, P. Ricerche sulla etiologia della encefalite epidemica con speciale riguardo ad un particolare virus filtrabile micrococciforme ed alla sua recettività per le scimmie (macachi). [**Investigations on the aetiology of epidemic encephalitis, with special reference to a peculiar micrococcus-like filter-passing virus and on its virulence for monkeys.**] *Arch. per le sc. med.*, 1921, **44**, 212.

The present paper is in part an enlarged repetition of another one to which reference is made above. But some interesting considerations and a description of the results obtained by the intracerebral inoculations into two monkeys of 1/10th of a loopful of a 48-hours' pure culture in serum agar of the 1920 virus are new. One of the two animals did not show any special symptoms, and the experiment was considered as negative. The other, a macacus, showed phenomena of general depression with slight fever and a sort of stupor which reached its maximum at the seventh day from the inoculation. During the following days a certain tendency to recovery was noticed, so that it was considered advisable to kill the animal ten days after the beginning of the experiment. From the brain and blood (collected from the heart) the same virus was re-obtained in pure cultures. The histological examination of the brain showed the presence of perivascular infiltrations chiefly due to lymphocytes and diffused to the hemispheres and basal grey formations.

According to Bastai this 1920 virus is similar to, but not identical with, that of Levaditi and Harvier, not only because it is obtainable in pure cultures and is morphologically recognizable as a very minute coccus, but also because experiments of cross-immunity, carried out by Bastai himself in Levaditi's laboratory, were attended by negative results. In addition, Levaditi and Harvier's virus is inactivated by bile, while that of the author resists such a treatment even when prolonged for 24 hours. And the action of this virus appears rather peculiar as regards transmission to rabbits by means of corneal scarifications. If a loopful of a pure culture in ascitic fluid is inserted in the scarified cornea of a rabbit, it only produces a slight local reaction. But the same quantity of the same material kills a rabbit within the first 24 hours when inoculated subdurally, and a fragment from the brain of this rabbit is fatal for a third one when smeared on its scarified cornea. The same happens if a fragment from the brain of the third rabbit is smeared on the scarified cornea of a fourth one; and so on indefinitely. Strangest of all appears to be the fact that in the nervous system of all these rabbits no macroscopic or microscopic lesions were seen. C. d. F.

Da Fano, C. (1). **A preliminary note on the histo-pathology of epidemic (lethargic) encephalitis.**] *Brit. M. J.*, 1921, i, 153.

Da Fano, C. (2). **Preparations from cases of epidemic (lethargic) encephalitis.** *J. Physiol. Proc. Physiol. Soc.*, 1921, **54**, cxiv.

Da Fano, C. (3). **On encephalitis lethargica.** *Brit. M. J.*, 1921, ii, 652.

In a previous communication on the same subject, published in collaboration with H. Ingleby (*Proc. Roy. Soc. Med.*, 1919, **12** (Path. Sect.), 42),

mention was made by the author of a granular pigment-like material occurring in the nerve-cells of regions of the central nervous system, where brown or black pigment is not usually found. It was also pointed out that in certain nerve-cells small, round, or oval bodies had been detected, in the middle of which a granule could be seen. The optical impression of such an appearance, when present in Bielschowsky or Nissl preparations, was that of a sort of halo surrounding each granule. When that note was written no more detailed description of such pictures was given, because it was only meant to be a short comment on a demonstration of preparations, and because the author was still uncertain as to the significance of such appearances. It was only later on that the careful examination of a great number of specimens convinced him that he had under observation something not, as far as he knew, hitherto described either in epidemic encephalitis or in other diseases of the central nervous system. As, however, the doubt of an optical illusion could not be entirely dispelled, no further communication was made on the subject, and he waited for an opportunity of some support for his conviction. This presented itself under the form of a few preparations which he was able to obtain in Paris through the kindness of H. Durand and C. Trétiakoff. The facts observed are illustrated by seven drawings and summarized in the following conclusion: in the nervous tissue from cases of lethargic encephalitis within and without the nerve-cells, minute bodies occur, to all appearance, consisting of a central basophil particle and of a delicate slightly stainable body, irregularly round or oval in shape. For these forms the term 'minute bodies' is suggested *pro tempore*. The bodies are generally discrete, and provided with one granule, but dumbbell-shaped forms occur as well as others with two central particles arranged in pairs. A relation, as yet indefinable, seems to exist between these forms and a pigment-like material occurring within the nerve-cells in places where brown pigment is not generally found. Minute forms, similar in shape, structure, and staining properties to those observed in the nervous tissue, have been traced within and without the cells infiltrating a salivary gland from an acute case of the disease. After discussing the supposition that such findings might be the product of an optical illusion associated, perhaps, with degenerative changes caused by the malady, the suggestion is tentatively put forward that they may be due to the presence in the tissues of a living agent, the cause of the disease.

In his second note the author briefly describes the method used for the demonstration of his 'minute bodies'. This consists of staining sections, from material fixed in alcohol and embedded in celloidin, either with 1 per cent. aqueous solution of toluidine blue or with Unna's polychrome methylene blue as by Nissl's method. There is only this difference, that the sections, freed whenever possible from all celloidin, are stained for a second and third time after having been each time completely differentiated with 96 per cent. alcohol. This repetition of staining and differentiating, particularly when carried out with relatively old solutions of toluidine blue, appears to have a double advantage. In the first instance, it greatly helps in imparting to the cytoplasm of nerve-cells, neuroglia cells, and other elements of the preparations, a more or less intense purple colour, on which differently stained parts, such as nuclei and granules, stand out sharply and definitely. In the second place it seems to render the specimens more resistant to the injurious influence of time. In sections from acute cases of lethargic encephalitis treated in the manner described, the central particle of the

supposed bodies is stained deep blue, the surrounding halo whitish-blue, while pigment granules appear coloured in various shades of green.

The third note is a contribution to a discussion in the sections of Medicine and Pathology and Bacteriology at the 1921 meeting of the British Medical Association. The author cautiously comments on his findings, and gives a brief preliminary description of an acute case of encephalitis in which the disease lasted less than three days. There was intense perivascular and interstitial infiltration of all parts of the central nervous system, but especially of the white matter of cerebral cortex and optic thalamus. In contrast to what is generally seen in encephalitis lethargica, the infiltration consisted of polymorphonuclear leucocytes and macrophages, with few lymphocytes and no plasma cells. C. d. F.

Salvioli. La febbre quintana o volinica. [**Trench fever.**] *Boll. d. Ist. Sieroterap. Milanese,* 1921, **2**, 47.

No new facts are described, but a general survey given of our present state of knowledge in regard to trench fever briefly summarized in the following conclusions: The malady is certainly infectious. The incubation period generally lasts from 12 to 25 days. The principal clinical types are the paroxysmal, the typhoid, and the rudimentary. The duration is variable; in the paroxysmal form exacerbations supervene every 8 or 10 weeks. No fatal cases appear to have ever been observed. The disease does not confer any immunity. The serum from patients agglutinates *Proteus* X 19. The aetiologic factor is the *Wolhynia rickettsia,* which can be found in the intestine of the transmitting agent, the louse, and in the circulating blood from patients during febrile exacerbations. C. d. F.

Frassi, L. Un caso di Sodoku. [**A case of rat-bite fever.**] *Atti di Soc. lomb. di sc. med. e biol.,* 1921, **10**, 73.

Mantovani, M. (1). Contributo all' eziologia del Sodoku. [**Contribution to the aetiology of rat-bite fever.**] *Pathologica,* 1921, **13**, 396.

Mantovani, M. (2). Ulteriore contributo all' eziologia del Sodoku. [**Further contribution to the aetiology of rat-bite fever.**] *Pathologica,* 1921, **13**, 423.

Frassi's patient was a woman whose right middle finger had been bitten by a rat a fortnight before being admitted into the hospital. The chief symptoms were remittent fever, a painful swelling similar to a ligneous phlegmon of the bitten finger, and conspicuous oedema of the whole right arm. The blood examination only showed a slight leucocytosis. There was no sign of syphilis. All bacteriological investigations were attended by negative results. The woman recovered after repeated injections of neosalvarsan.

Mantovani's first case was that of a child who had been bitten by a rat (*Mus decumanus*). The author does not give any clinical details of this case, but a brief account of various bacteriological investigations summarized in the following conclusions: (1) The infection was certainly due to a spirochaete similar to, if not identical with, that described by Futachi, Ishiwara, and other authors (*Spirochaeta morsus muris*). (2) In the blood from the patient and in the blood and various organs from guinea-pigs experimentally infected, two kinds of spirochaeta were noticed, one short with corkscrew-like spirals and flagellated, one thin and long and without flagella. (3) In many of the

infected guinea-pigs a swelling of lymph-glands and suprarenal glands and a congestion of all organs were noticed. Some of the animals showed a haemorrhagic syndrome similar to that seen in cases of spirochaetosis ictero-haemorrhagica, but without jaundice.

Mantovani's second case was a woman 64 years of age, whose right little finger had also been bitten by a *Mus decumanus*. Fever developed in exacerbations supervening every three days and accompanied by headache, severe gastro-intestinal troubles, and acute pains spreading from the right arm to the trunk and legs. No sign of syphilis. Wassermann's reaction negative. The patient recovered after injections of neosalvarsan. The results of bacteriological investigations were similar to those obtained in the former case. It was, in addition, observed that the short forms of spirochaeta prevailed in the blood from infected guinea-pigs, mice, and one cat, while the long and slender ones were chiefly found in organs and in cultures obtained on haemolysed rabbits' serum. The infection could be transmitted in series from guinea-pig to guinea-pig, in which it gave origin to a haemorrhagic syndrome accompanied after the seventh passage by an intense jaundice, so that the animals seemed affected by spirochaetosis ictero-haemorrhagica. The author puts forward the suggestion that this form and rat-bite fever may be closely related as far, at least, as the aetiological factor is concerned. C. d. F.

Reichenow, E. Untersuchungen über das Verhalten von *Trypanosoma gambiense* im menschlichen Körper. [**On the behaviour of *Trypanosoma gambiense* in the human body.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 266–385.

This is an exhaustive account of the behaviour of *Trypanosoma gambiense* in the human body. The special points dealt with, including the periodicity of the parasites in the blood and its cause, the trypanosoma in the cerebrospinal fluid, the changes brought about in the fluid, and the course of the infection. While most of the paper is of interest, especially to students of tropical medicine, the analogy of the changes brought about by *T. pallidum* and *Trypanosoma gambiense* in the central nervous system is of general interest. In both infections the C. S. F. is invaded early, and there is a latent period which, however, in the case of syphilis is of much longer duration and is more insidious. Apparently, the virulence of *T. pallidum* in the C. S. F. is very much less than that of *Trypanosoma gambiense*.

W. B.

Luger, A., Lauda, E., u. **Silberstern, E.** Das Krankheitsbild der experimentellen herpetischen Allgemeininfektion des Kaninchens. [**The clinical picture of generalized experimental herpes in the rabbit.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 200.

The authors carried out inoculations, in the cornea of thirteen rabbits, with the contents of the vesicles of herpes febrilis. Seven yielded a positive result after an incubation period which had an average duration of seven to fourteen days. Even during the incubation period the authors noted that the animals were restless, excitable, and trembling. General symptoms then set in, and in five cases ended in death. Emulsions of cerebrospinal tissue of the fatal cases induced infection after intravenous or intraneural inoculation. The general symptoms manifested themselves in two forms, the

one of short duration with paroxysms, the other more protracted. The blood and brain and splenic emulsions caused inoculation keratitic herpes in other rabbits. W. B.

Luger, A., u. **Lauda, E.** Ein Beitrag zur Frage der Übertragbarkeit des Herpes zoster auf das Kaninchen. [**A contribution to the question of the transmissibility of herpes zoster to the rabbit.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1921, **94**, 206.

With the contents of the vesicles of seven cases of herpes zoster the authors found, in contrast to herpes febrilis and herpes corneae, that there were no characteristic changes in the corneae of rabbits. A previous inoculation with the vesicular fluid from zoster induced no immunity to a subsequent inoculation on the cornea with the contents of vesicles of herpes febrilis. No general symptoms followed inoculation of zoster fluid. The 'zoster bodies' described by Lipschütz were found in the human but not in rabbit lesions. W. B.

Teissier, P., Gastinel, P., et **Reilly, J.** Présence d'un virus kératogène dans les herpès symptomatiques. L'unité des herpès. [**The presence of a keratogenic virus in symptomatic herpes. The unity of herpes.**] *Compt. rend. Soc. de biol.*, 1922, **86**, 73.

The authors briefly state that the contents of herpes vesicles occurring in the course of different diseases are inoculable on the cornea of rabbits. They have had positive results with herpes from cerebrospinal meningitis, acute pneumonia, diphtheria, influenza, benign jaundice, angina erythematosa of undetermined origin, and mumps. They also demonstrated the virus in a herpes genitalis in a patient suffering from secondary syphilis. In most cases the inoculated rabbits succumbed. They regard the occurrence of herpes in the several above-mentioned diseases as a complication, the one infection being superposed on the other. They draw attention to the rarity of herpes in scarlatina, variola, and varicella. W. B.

Teissier, P., Gastinel, P., et **Reilly, J.** La transmission du virus herpétique au rat blanc. [**The transmission of the virus of herpes to the white rat.**] *Compt. rend. Soc. de biol.*, 1922, **86**, 75.

In general, the rat has been considered as insusceptible to herpetic virus. The authors show that this is not so, although the lesion on the cornea is often transient and slight. Even although the keratitis may be absent the virus may penetrate into the central nervous system and may be propagated by passage both in rats and in rabbits. W. B.

Olitsky, P. (1). **Experimental studies on the etiology of typhus fever. I. Concurrent infections during the course of experimental typhus fever in guinea-pigs.** *J. Exper. M.*, 1921, **34**, 525.

Olitsky, P. (2). **Experimental studies on the etiology of typhus fever. II. Survival of the virus in aerobic and anaerobic culture media.** *J. Exper. M.*, 1922, **35**, 115.

Olitsky, P. (3). **Experimental studies on the etiology of typhus fever. III. Filtration experiments.** *J. Exper. M.*, 1922, **35**, 121.

In the first of these papers the author gives his results with the inoculation of two strains of typhus fever virus in guinea-pigs. During the early

stages of the experimental infection the virus can be obtained free from admixture with any ordinary bacteria, although the latter have a tendency to invade the body and may complicate the results. Even on the first day of the fever the bacilli of Plotz were recovered twice and anaerobic streptococci, *B. proteus*, aerobic diphtheroids, Gärtner-type bacilli, and *S. pyogenes aureus* each once. None of these microbes have, however, any aetiological relation to the disease. In the second paper experiments are described to determine the viability of the typhus virus under aerobic and anaerobic conditions. At 37° C. the virus was found to survive longer in aerobic than in anaerobic cultures, but in neither case was the organism alive after five days. In the third paper attempts are described to determine whether the virus is intracellular and whether it is filterable. Working with infected spleen and brain from guinea-pigs, it was found that the virus does not lose its infecting power when the cells are disintegrated by repeated freezing and thawing, by freezing and drying, by mechanical crushing, or by grinding with sand. Fourteen attempts, to filter through Berkefeld V and N bougies the virus contained in the disintegrated tissue, were all negative.

W. B.

Duval, C. W., and **D'Aunoy, R. Studies on experimental measles. I. The effects of the virus of measles upon the guinea-pig.** *J. Exper. M.* 1922, **35**, 257.

Blood was taken from seven cases of measles in the eruptive stage of the disease, and, after being defibrinated, was injected in doses of 2 c.cm. into the hearts of guinea-pigs. Of 28 animals treated in this way 20 showed reactions consisting of pyrexia, leucopenia, and nephritis after an incubation period of 9 to 12 days. The reaction in the guinea-pig is produced with human blood corresponding to the eruptive stage of the disease. Thirty-six hours prior to the rash and 24 hours after defervescence the blood of cases of measles is innocuous. Animals which react and recover are not susceptible to reinoculation of measles blood up to three months after recovery. Normal human blood injected intracardially produces no leucocytic or temperature changes. These results led the authors to conclude that it was possible to transmit the virus of measles to guinea-pigs, and that by passage through these animals the virus is exalted and may end in death from acute haemorrhagic nephritis. No exanthem was seen, and coryza and injection of the buccal mucous membrane was inconstant.

W. B.

BIOCHEMISTRY

Ghose, S. N. The examination of some Indian foodstuffs for their vitamin content. *Biochem. J.*, 1922, **16**, 35.

A sample of pure Indian 'ghee' proved to be as good a source of vitamin A as pure butter. Remelted 'ghee' failed to restore growth in rats whose weight had become stationary on a shortage of fat-soluble A. More adulterated 'ghees' only gave growth when administered in large quantities. Certain vegetable oils, e. g., coco-nut oil, and pure mustard seed

oil, gave growth when they formed 10 to 20 per cent. of the basal diet. Lentils had a considerable quantity of vitamin B. Bleached Indian flour is deficient in vitamin B. Crude 'atta' and unbleached Indian flour have considerable quantities of water-soluble vitamin B. C. G. L. W.

Silva, S. S. Conditions of inactivation of the accessory food factors. *Biochem. J.*, 1922, **16**, 42.

The fat-soluble factor in cod-liver oil was destroyed by exposing it to ozone in the dark at ordinary temperatures, and by bubbling air through it at 120°. Autolysed yeast juice retained its activity when treated with ozone in the dark. The antiscorbutic activity of decitrated lemon juice is destroyed by ozone and also by air at ordinary temperatures. Ultra-violet rays have no deleterious action on the accessory fat factor in the absence of air. The antiscorbutic potency of decitrated lemon juice is not destroyed by boiling in an atmosphere of carbon dioxide, whereas one hour's boiling in the presence of air almost entirely destroyed its potency. The treatment of lemon juice by hydrochloric acid for 5 hours gave a product which retained much of its activity. C. G. L. W.

Eijkman, C., Van Hoogenhuyze, C. J., and **Derks, T. J. G. The vitamin content of microorganisms in relation to the composition of the culture medium.** *J. Biol. Chem.*, 1922, **50**, 311.

It has been rather tacitly assumed that the water-soluble B substance (capable of promoting the growth of young rats), and the antineuritic factor (curing avian polyneuritis), are identical. This assumption is now being questioned. Nelson, Fulmer and Cessna showed recently that yeast grown upon simple synthetic media, namely, mineral salts, ammonium chloride, and cane sugar were able to synthesize water-soluble B. Eijkman and his colleagues have shown on the other hand that yeast cultivated upon a medium not containing the antineuritic vitamin, is free of antineuritic vitamin. *B. coli communis* will not synthesize antineuritic vitamin even when grown upon a medium containing it. The evidence therefore points to a real difference between the two vitamins.

An interesting secondary question is raised by the observation that a yeast grown upon a medium containing antineuritic vitamin, even after inactivation by heat, is found subsequently to contain the vitamin.

R. A. P.

Daniels, A. L. Can yeast be used as a source of antineuritic vitamin in infant feeding? *Am. J. Dis. Child.*, 1922, **23**, 41.

Two to ten grammes of air-dried pulverized yeast, soaked and boiled, were given to healthy children. In some cases growth was apparently stimulated, but in others diarrhoea was produced with resultant loss of weight.

O. L. V. de W.

Hutchison, H. S. The aetiology of rickets, early and late. *Quart. J. Med.*, 1922, **58**, 167.

Rickets, both early and late, is not an uncommon complaint in India. The disease occurs almost exclusively among the well-to-do classes, and appears to be the result of the purdah form of life, which leads to lack of

fresh air, sunlight and exercise. The purdah classes consume a diet containing a fair amount of milk and clarified butter. Among the poorer classes, whose diet is very deficient in fat-soluble vitamin, but who live largely in the open air, rickets is extremely rare. O. L. V. de W.

McCann, W. S. The protein requirement in tuberculosis. *Arch. Int. Med.*, 1922, **29**, 33.

In 10 tuberculous patients determinations were made of the nitrogen balance, the basal metabolism, and the caloric value and composition of the diet. In 9 of these cases the minimal urinary nitrogen excretion observed was between 2·5 and 4·5 gm. per diem (0·041 to 0·093 gm. per kilo). In one case of acute pneumonic phthisis, the lowest urinary nitrogen excretion was 9·4 gm. per diem (0·267 gm. per kilo). In the 9 cases with a minimal nitrogen excretion the diet had an energy value from 1·1 to 2·4 times the basal requirement of the subject. Some cases are able to attain nitrogen equilibrium, or even a positive N balance, on diets containing 37 to 44 gm. protein, provided that carbohydrate and fat are given in sufficient quantities to make the total caloric value of the diet up to 1·7 to 2·4 times the basal energy requirement. The evidence indicates that the optional amount of protein for patients suffering from pulmonary tubercle and confined to bed is from 60 to 90 gm. per diem., with a total caloric value for the diet of about 2,500 calories. O. L. V. de W.

Hill, R. M., and **Lewis, H. B. The hydrolysis of sucrose in the human stomach.** *Am. J. Physiol.*, 1922, **59**, 413.

The inversion of cane sugar in the human stomach is due to the acid and varies with the concentration of the acid. Normally the amount of cane sugar inverted is slight, as it leaves the stomach too rapidly to permit of prolonged action of the acid. W. C.

Knaffl-Lenz, E. Über Darmsaccharase. [**The saccharase of the intestine.**] *Ztsch. f. physiol. Chem.*, 1922, **119**, 60.

The mucous membrane of the gut causes the inversion of cane sugar, while pure intestinal juice has no such action. The author does not think the view that the invertase is an endo-enzyme is a satisfactory explanation. He suggests that the proteolytic enzymes present in the intestine may rapidly destroy any saccharase which may be secreted. H. W. D.

Demuth, F. Motilitätsprüfungen mit Eiweiss, Fett und Kohlenhydraten am kranken Magen. [**Motility tests with protein, fats, and carbohydrates in diseases of the stomach.**] *Deutsches Arch. f. klin. Med.*, 1921, **137**, 292.

The time of evacuation of the stomach was observed by mixing barium sulphate with various types of food, and the following results obtained. In meals of equal size the time of emptying is shortest in those meals in which carbohydrates are predominant. The longest time is taken by a meal high in fat. With anacidity the time of retention is smallest with carbohydrate meals. Both in carcinoma and probably in gastric ulcer, the time of retention was prolonged so that the carbohydrate meal remained in the stomach a longer time than does fat under normal conditions.

C. G. L. W.

Michaelis, L., u. Müller, F. Eine Indikatorenmethode zur Aciditätsmessung im Magen- und Darm-Saft beim Erwachsenen und beim Säugling. [**The indicator method for determining acidity in stomach and intestinal contents in adults and infants.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 149.

By the use of crystal violet, α, β, and γ dinitrophenol and p- and m-nitrophenol the authors have constructed a set of indicators which covers the entire range of acidity of gastric contents in normal and pathological conditions. The details must be consulted in the original. C. G. L. W.

Isaac-Krieger, K. Zur quantitativen Bestimmung der Fermente im Duodenalsaft. [**Quantitative estimation of the ferments in the duodenal secretion.**] *Ztschr. f. klin. Med.*, 1921, **92**, 259.

By the use of the duodenal sound and an estimation of the amount of trypsin diastase and lipase in the fluid recovered one may obtain information regarding the capacity of the pancreas to produce a normal pancreatic juice. It would appear that a decrease in the amount of ferment content in the juice below certain values, which must be seen in the original (because they depend upon standard methods of estimation), are indicative of a disturbance in the external secretion of the pancreas and the method is therefore of considerable service in estimating the functional capacity of this organ.
C. G. L. W.

Hartwell, G. A. Mammary secretion. III. 1. The quantity and quality of dietary protein. 2. The relation of protein to other dietary constituents. *Biochem. J.*, 1922, **16**, 78.

Large quantities of protein fed to a nursing rat are detrimental to the young, even when the diet contains all the essential constituents. If the diet is started at birth some of the litter may survive, but they are not normal. If the diet is begun on or before gestation none of the young survive. It is suggested that toxic substances in the milk affect the young at some special state of development. The bad effects are entirely obviated by adding 100 c.cm. of whole milk to the mother's diet. C. G. L. W.

Currie, A. N. The fat of adipose tissue in malignant disease. *J. Path. & Bacteriol.*, 1922, **25**, 213.

There is a constancy in iodine value of normal adipose tissue fat from any part of the body. The fat pigment tends to preserve the unsaturation equilibrium of the fat in adipose tissue: the more highly pigmented the fat the greater is its resistance to catalytic hydrogenation. In malignant disease marked differences are found in the iodine value of adipose tissue fat; the fatty unsaturation is most marked in local carcinomatous fats, less in local sarcomatous fats, and less still in fat from the neighbourhood of chronic inflammatory lesions. The same order of iodine values applies to the distant fats in these conditions, but the distant fats show a lower degree of unsaturation than the local fats. O. L. V. de W.

Hatieganu, J. Un nouveau procédé pour l'examen de la fonction sécrétoire du foie. [**A new method of examining the secretory function of the liver.**] *Ann. d. méd.*, 1921, **10**, 400.

The excretion of colouring matters in the bile was studied by means of the duodenal sound. Methylene blue subcutaneously injected proved valueless. The author then employed 0·16 to 0·24 gm. indigo carmine in 20 c.cm. of saline solution. This dye was found to appear in the duodenal contents in 20 minutes, and excretion continued for 9 to 10 hours. Excretion was absent or retarded in diseases of the liver. In diabetics, a hyper-permeability of the liver appeared to be present. O. L. V. de W.

Wisner, F. P., and **Whipple, G. H. Variations in output of bile salts and pigments during 24-hour periods. Observations on standard bile fistula dogs.** *Am. J. Physiol.*, 1922, **60**, 119.

Observations on three dogs with biliary fistulas over prolonged periods show that during four consecutive six-hour periods there is a fairly constant output of bile, bile salts, and pigments. A large dose (2 gm.) of crude taurocholic acid produces an immediate rise in the excretion of bile salts so that practically all the taurocholic acid given is excreted within the six hours after its ingestion. The volume of bile is also greatly increased. During the second six-hour period the bile-salt content is about normal, but the volume of bile remains above that level. The excretion of bile pigment is unaltered throughout. The fluid output is therefore to a certain extent dissociated from that of the bile salts.

An interesting effect which was observed on autopsy in two of the dogs is that the bones were profoundly affected, The costochondral junctions were enlarged, the ribs were fragile and almost destitute of lime salts and gave evidence of healed spontaneous fractures. The two dogs in which these changes were found are described as 'young'. The third dog did not show bone changes and emaciation found in the other two. This dog was six years old, and exclusion of the bile from the duodenum was incomplete. W. C.

Cori, G., u. **Mautner, H.** Der Einfluss der Lebergefässe auf den Wasserhaushalt und die hämoklasische Krise. [**The influence of the hepatic vascular system on the excretion of water and the 'crise hémoclasique'.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 301.

It has been shown that the lymphatic venous system of carnivora differs from that of herbivora in that the veins contain a muscular mechanism whereby the flow of blood from the organ can be regulated and hence the concentration, viscosity, and other physico-chemical properties of the blood can be kept at a definite level. Widal has studied a condition which he calls the 'crise hémoclasique' which occurs in asthma, urticaria, and in other conditions, e. g. cirrhosis of the liver. This crisis is said by Widal to be due to a flooding of the organism with breakdown products of protein which occasions a spasm of the lymphatic veins causing a fall in blood-pressure. This crisis is also produced by administering water. The authors have investigated the effect of administering 10 c.cm. of pathological saline intravenously to children. With normal subjects a leucocytosis occurs. In disturbances of the liver there is a leucopenia. This also takes place when 150

to 500 c.cm. of water are given *per os*. They believe that the mechanism by which spasm is produced in the hepatic veins is one which regulates the water economy of the organism and is intimately concerned in the production of the 'crise hémoclasique'. It may be produced by decomposition products or by water. The normally functioning liver has a mechanism to compensate for this spasmodic contraction of the veins. C. G. L. W.

Eppinger, H. Zur Chemie der amyloiden Entartung. [**On the chemistry of amyloid degeneration.**] *Biochem. Ztschr.*, 1922, **127**, 107.

An amyloid liver tumour was found to contain a proteid body. Analysis showed that this was free from cystine and histidine, but contained large quantities of diamino acids. It appeared to contain purine bodies but not carbohydrate. R. A. P.

Kramer, B., Tisdall, F. F., and **Howland, J. The clinical significance of calcium concentration in the serum of children, and possible errors in its determination.** *Am. J. Dis. Child.*, 1921, **22**, 560.

In normal children the calcium concentration varies from 10 to 11 mgm. per 100 c.cm. of serum. Thirty-one cases of tetany showed an average concentration of 5·8 mgm., fifty-six cases of rickets 8·6 mgm., and in twelve out of twenty cases of nephritis the calcium figure was found to be low. In no other pathological condition studied was any significant change in the calcium concentration found. O. L. V. de W.

Pelkan, J. F., and **Whipple, G. H. Physiology of the phenols. II. Absorption, conjugation, and excretion. III. Phenol conjugation as influenced by liver injury and insufficiency.** *J. Biol. Chem.*, 1922, **50**, 499.

A new method for analysing the phenols in the blood, (Pelkan) has been directed to the problem of the conjugation of the phenols with sulphate in the body. Intravenous injection into dogs of large doses of phenol and *p*. cresol (up to 500 mgm.), leads to violent toxic symptoms which soon pass off. There is found to be a rapid distribution of the administered phenol in the body so that the concentration of free phenol falls very rapidly in the blood, reaching the normal value in about 60 minutes. Concurrently with this there is a rise in the amount of conjugated phenol. Quite different results are obtained in the case of ingested phenol. The rise of free phenol in this case is comparatively slight, only lasting in the case of severe doses a matter of 30 minutes. The doses given this way do not induce toxic symptoms. The conjugated phenols show a rise lasting 1–2 hours. This suggests, as has been held previously, that the main conjugation takes place in the liver—a view which is confirmed in the third paper of the series, where it is shown that the production of an Eck fistula reduces the amount and speed of conjugation of phenol. If the liver circulation is impaired by further ligature of the hepatic artery, the phenol conjugation may be reduced to 5 per cent. of the normal. Extensive liver lesions by chloroform and phosphorus may reduce the conjugation even to zero. From this it is concluded that the liver is the sole seat of phenol conjugation in the body. Its function is supposed to come into play, whenever the amount of phenol substances coming from the intestine becomes too great to be dealt with by an oxidative mechanism. R. A. P.

Barach, A. L., Means, J. H., and **Woodwell, M. N. The hydrogen-ion concentration and bicarbonate level of the blood in pneumonia.** *J. Biol. Chem.*, 1922, **50**, 413.

A study of the above has been made in 10 cases of pneumonia. In three observations were obtained before and after the crisis. No definite correlation was obtained between the dissociation curve level (obtained from the amount of CO which will combine with the blood at 40 mm. tension of gas) or the hydrogen-ion concentration, and the degree of anoxaemia or the prognosis. As a matter of fact the lowest values of P_H and of the dissociation curve level obtained were lower than the normal, but others were normal. A change was observed at the crisis in the sense of a return of the P_H and of the dissociation curve to the normal. The same was also observed without crisis after vigorous treatment with oxygen. As suggestions for treatment arising out of their work, the authors think that in pneumonia patients who show either a low level of available blood alkali or a decrease in the hydrogen-ion concentration, the administration of sodium bicarbonate should prove useful. It is important, however, to combat any anoxaemia with oxygen therapy. Otherwise a diminution in the acidity of the blood might lead to a less degree of pulmonary ventilation and so to an exaggeration of the lack of oxygen. R. A. P.

Turban, K. Vergleichende Untersuchungen über den Blutzuckergehalt des arteriellen und des venösen Gefässsystems. [**Comparative experiments on the sugar content of arterial and venous blood.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 4.

Arterial blood contains more sugar than venous blood in both normal and fasting animals. H. W. D.

Cohn, E. A. Über das Verhalten des Reststickstoffs im Blute bei Grippe. [**The rest nitrogen of the blood in influenza.**] *Ztschr. f. klin. Med.*, 1921, **92**, 201.

The rise in the rest nitrogen of the blood was observed in 53 per cent. of 150 cases examined. In one case the very high value of 157 mgm. per 100 c.cm. of blood was obtained. It is looked upon as due to a true toxic decomposition of protein. Neither clinically nor anatomically were changes in the kidneys observed. If the rest nitrogen rises quickly it is looked upon as a serious prognostic sign. C. G. L. W.

Travers, P. Über das Verhalten des Blutzuckers bei Herzkranken unter besonderer Berücksichtigung der therapeutischen Anwendung von intravenösen Traubenzuckerinfusionen. [**The blood-sugar in disease of the heart and the therapeutics of intravenous glucose administration.**] *Deutches Arch. f. klin. Med.*, 1921, **137**, 284.

Büdingen reported in 1914 on the good results obtained by the intravenous infusion of glucose solution in heart disease, which he attributed to the direct influence of the glucose on the heart muscle. He explained this as due to a reserve of glycogen being produced in the muscle itself. He called the condition in which the glucose produced this good effect a 'cardiodystrophia hypoglycaemica'. The present author has not been able to confirm Büdingen's results, but he believes that the use of intravenous sugar

infusion in cases of compensated heart lesions is a distinct advance in therapy. The use of 10–20 per cent. glucose solution in many other conditions associated with loss of strength or haemorrhage, or loss of water is undoubtedly to be recommended and is preferable to the use of isotonic saline. C. G. L. W.

Brösamlen. Die Adrenalinhyperglykämie. [**Adrenalin hyperglycaemia.**] *Deutsches Arch. f. klin. Med.*, 1921, **137**, 299.

While adrenalin always produces a hyperglycaemia when injected subcutaneously, a glycosuria was only found four times in 35 experiments. In each case the subject was pathological. The hyperglycaemia always takes place much later than the effect which the drug produces on the pulse and blood-pressure. The high point of the blood-sugar curve occurs at a time when both pulse and pressure have practically regained their normal level. The blood-sugar curves in diabetics were not always similar. In some there was a fall in the amount of sugar in the blood which afterwards rose slowly. In other cases the hyperglycaemia was very pronounced, even more so than in healthy subjects. It is possible that an analysis of these curves might lead to a separation of cases of diabetes which are, on the one hand, of pancreatic origin and, on the other, are due to nervous disturbance. C. G. L. W.

Olmsted, W. H., and **Gay, L. P. Study of the blood-sugar curves following a standardized glucose meal.** *Arch. Int. Med.*, 1922, **29**, 384.

The individuals tested were examined after a 12-hour fast. For each kilo of body-weight 1·75 gm. of glucose were given, and the sugar estimated at intervals of one hour for three hours. Sustained hyperglycaemias were found in furunculosis, in cases of gastro-intestinal neoplasms, especially if metastasis were present, and the arthritis after injection of foreign proteins. In hyperthyroidism the curves obtained were high, but fell rapidly. The height of the curve bore no relationship to the basal metabolism. In hypothyroidism, and in hypopituitarism the curves ran low. In one case of Addison's disease a low curve was obtained. O. L. V. de W.

Mills, C. A., and **Mathews, S. Influence of blood serum on the coagulative activity of tissue extracts.** *Am. J. Physiol.*, 1922, **60**, 193.

Rabbit serum greatly increases the coagulating activity of tissue (lung) extract. The increase may be as high as thirty-fold. This increase takes place at once when the two are mixed, and gradually diminishes as the mixture is allowed to stand. Human serum, normal and syphilitic, shows the same phenomenon. It is suggested that this phenomenon may have an important bearing on the sudden reaction produced sometimes by the intravenous injection of organ extracts or serum, which may be harmless alone, but may be activated sufficiently by the patient's blood to become exceedingly toxic. W. C.

Gratia, A., and **Levene, P. A. The role of cephalin in blood coagulation.** *J. Biol. Chem.*, 1922, **50**, 455.

Older workers, owing to the difficulty of separating the phosphatides, thought that lecithin was the thermostable factor in blood coagulation

(called 'kinase' in the Morawitz nomenclature). More recently Howell thought that the real agent was not lecithin but cephalin, another phosphatide. Gratia and Levene have shown that neither pure egg lecithin nor pure liver lecithin have effect in blood coagulation, but that as little as 1/20,000 mgm. of cephalin may be effective. This confirms Howell's view of the nature of this substance. (For a discussion of views upon coagulation the reader is referred to *Medical Science*, 1922, **5**, 496; **6**, 49.) R. A. P.

Underhill, F. P., and **Ringer, M.** **Studies on the physiological action of some protein derivatives. V. The relation of blood concentration to peptone shock.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 163.

While it is well known that blood-volume changes are bound up with shock, the details of this relationship have not been extensively investigated. Fasting dogs were injected intravenously with solutions of Witte's peptone, and the blood-pressure and the haemoglobin percentage were estimated. The experiments were controlled by purified proteoses and by histamine. The shock produced by peptone is similar to that effected by histamine except that the period of high concentration of the blood is higher with the latter drug. It would appear that the damage to the capillaries is greater when peptone is used for injection, and hence the recovery is slower.
C. G. L. W.

Underhill, F. P., and **Errico, L.** **The influence of purgatives on blood concentration.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 135.

Saline purgatives produce in dogs a distinct concentration of the blood. The maximum effect is reached during the second hour. Although diarrhoea occurs during the fourth and sixth hours by the use of vegetable purgatives (castor oil, cascara sagrada), no change in the haemoglobin content occurs. The authors state that in pathological cases where the blood is known to be concentrated, harm may be done by the administration of saline purgatives. This may account for the collapse which is sometimes seen when these drugs are administered. C. G. L. W.

Jeanselme, E., et **Pomaret, M.** Étude expérimentale des phénomènes de choc produits par les arsénos et novarsénobenzènes. [**Experimental study of shock produced by arseno- and novarsenobenzol.**] *Ann. d. méd.*, 1921, **10**, 167.

An investigation of the causes of the nitritoid crisis, as seen in the fall of arterial tension in dogs after injections of these bodies. The authors conclude that the crisis is not due to any direct toxic action, but believe that it arises from a disturbance of the colloidal equilibrium of the blood, with resultant flocculation. O. L. V. de W.

Oliver, J., and **Douglas, E.** **Biological reactions of arsphenamine. I. The mechanism of its agglutinative action on red blood cells *in vitro*.** *J. Pharmacol. & Exper. Therap.*, 1922, **19**, 187.

Oliver, J., and **Yamada, S. S.** **II. The protective action of hydrophilic colloids on the agglutination of red blood cells by arsphenamine.** Ibid., 189.

The authors believe that the ill effects following salvarsan injection are partly due to agglutination of the red blood-cells by the drug. Human cells

are most strongly acted upon. Salvarsan is adsorbed by red cells, but no agglutination occurs except in the presence of electrolytes. A physical change in the degree of dispersion of salvarsan results when an electrolyte is added to its solution. In the second paper the protective action of hydrophilic colloids has been studied. They show that the same effect on salvarsan is induced as on colloidal gold, and an inhibition of the action of both the union of salvarsan with the red cells and of the action of electrolytes with the drug takes place. C. G. L. W.

Bieling, R., u. **Isaac, S.** Experimentelle Untersuchungen über intravitale Hämolyse. II. Der Verlauf der intravitalen Hämolyse nach Milzexstirpation. [**Intravital haemolysis. II. Haemolysis after extirpation of the spleen.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 251.

The injection of haemolytic immune sera produces the same effects in animals in which the spleen has been excised as in normal animals. No compensating action on the part of other organs is observed.

C. G. L. W.

Greene, C. W., and **Gilbert, N. C. Studies on the responses of the circulation to low oxygen tension. VI. The cause of the changes observed in the heart during extreme anoxaemia.** *Am. J. Physiol.*, 1922, **60**, 155.

In previous investigations the authors have examined in man the changes in the heart that occur in anoxaemia. In the present paper they have tested their conclusion by experiments on anaesthetized dogs. A progressive anoxaemia was induced by rebreathing air from a chamber in which the CO_2 was absorbed by alkali. Most previous observers had concluded that the asphyxial strain acted directly on the cardiac tissue and produced heart-block. The authors in confirmation of their observations on man find that the primary effect of oxygen want on the activity of the heart is due to vagospasm. The lack of oxygen leads to a stimulation, then suppression of respirations, and to a profound increase in activity of the vagal centre, either overlapping or quickly following the stage at which respirations cease. If the vagi are not injured during the progress of anoxaemia, the cardiac slowing during the three to five minutes immediately following respiratory failure is due to suppression of the S-A rhythm by vagal inhibition, while the A-V rhythm maintains itself until anoxaemia approaches a direct fatal effect. When this stage has been passed and the blood-pressure approaches zero, then a second and direct disturbance of the heart rhythm occurs which is due to heart-block. This is the stage observed previously by investigators who employed a more abrupt method of inducing asphyxia. With the vagi cut the first stage of cardiac slowing does not occur.

The cardiac slowing during the first 3–5 minutes after respiratory failure which is due to vagospasm can be promptly abolished by supplying oxygen, and respiratory and circulatory efficiency is then re-established.

The important practical application is that in man asphyxiation by anoxaemia has a considerable margin of safety, provided only that a few whiffs of oxygen can be introduced into the lungs within the 3–5 minutes' interval following respiratory collapse during which the heart continues to beat. W. C.

Winkin, C. S. An analysis of the nervous control of the cardiovascular changes during occlusion of the head arteries in cats. *Am. J. Physiol.*, 1922, **60**, 1.

Occlusion of the head arteries gives a complete anaemia of the brain. To this the organism responds by a series of vigorous reactions of which the most prominent is a prolonged rise of blood-pressure. This response was analysed experimentally in cats under artificial respiration. The response is controlled essentially by the splanchnic nerves. It is abolished by lesions which interrupt completely the continuity between the medulla and the coeliac ganglion, that is to say, either by section of the splanchnics before they enter the coeliac ganglion, or by section of the spinal cord high up in the thoracic portion. The level at which the splanchnic outflow leaves the spinal cord differs in different individuals. Most of the fibres leave the cord in the region of the sixth to eighth thoracic. Some fibres, however, leave the cord higher up, and in some individuals they may leave at the high level of the second or third thoracic.

Ligation of the adrenal glands does not prevent the response but modifies it somewhat. This fact is interpreted as signifying that the activity of the adrenal gland contributes to the rise in blood-pressure. This adjuvant action, however, is stated to be due not to an increased liberation of adrenalin from the adrenals, but depends on the amount of circulating adrenalin. It is also believed that there is evidence of some other product of adrenal activity appearing in intact animals as the result of repeated extreme splanchnic stimulation.

The most important conclusion is that the vasomotor response through the sympathetic is completely dependent on the integrity of the brain-stem and the maintenance of conductivity within it. The vasomotor responses transmitted by the sympathetic nervous system, are in respect to their complete dependence on the higher nervous levels of the central nervous system, comparable with skeletal responses. In other words, the central nervous system is not 'autonomic'. W. C.

Wieland, H. Über die Bedeutung des Calciums für die geringe Empfindlichkeit der Kröte gegen Herzgifte. [**On the importance of calcium for the small sensitivity of the toad to heart poisons.**] *Biochem. Ztschr.*, 1922, **127**, 94.

Bufotalin, the poison from the toad, is 30 times more poisonous to the grass frog than to the toad. Digitoxin and strophanthin behave in a similar way. The action of these three substances is different in the case of the toad; they cause diastole instead of systole. The same change is produced in a toad's heart by an increase of Ca, the reverse of the effect found in the frog's heart. Strophanthin has been shown to make the frog's heart more sensitive to the action of Ca, so that the difference in the behaviour of the hearts of the two animals to bufotalin becomes more intelligible. Both hearts behave in the same way to barium. R. A. P.

Neumann, R. Die Bedeutung des Katalaseindexes für die Diagnose der perniziösen Anämie. [**The significance of the catalase index in the diagnosis of pernicious anaemia.**] *Deutsches Arch. f. klin. Med.*, 1921, **137**, 324.

Van Thienen has observed that the catalase index is raised in cases of pernicious anaemia. This quotient is obtained when the number of millions

of the red cells is divided by the catalase number. This latter is got by acting upon a hydrogen peroxide solution with 0·05 c.cm. of blood and obtaining the amount of hydrogen peroxide decomposed in this way under standard conditions. It is, in effect, the amount of hydrogen peroxide in grammes that is decomposed in 30 c.cm. of a 1 per cent. solution by 1 c.cm. of blood which has been diluted with physiological salt solution 1,000 times. The author finds a fairly close concordance with the results of Van Thienen. He finds that the index in normal subjects is fairly constant, the average value is 4·16. It varies between 3·0 and 4·8. In secondary anaemias Neumann found values between 2·5 and 7·5. Van Thienen found much more constant indices. In pernicious anaemias, values 3 to 4 times the normal were obtained, but they were not constant. In some cases quite normal values occurred. The high numbers were only obtained in the severest phases of pernicious anaemia. It does not seem possible to differentiate between the cryptogenetic pernicious anaemias and the true ones with a known aetiology. On the other hand the author believes that when a distinct rise in the index is present it is a sure sign of a pernicious anaemia. C. G. L. W.

Block, W. Die praktische Verwertbarkeit der Amylase (Diastase)-Bestimmung in Blut und Urin für die Diagnostik der verschiedensten Krankheiten. [B.] [**The value of the diastase test in blood and urine for general diagnosis.**] *Ztschr. f. klin. Med.*, 1921, **93**, 381.

On the basis of a critical review of the literature, the author comes to the following conclusions. The diastase test should always be performed in blood and urine. Any renal disease should be excluded if other pathological conditions are to be investigated. As a test of kidney function it cannot be used alone. Only very large deviations from normal values are of any service for diagnostic purposes. If the values are less than 100 per cent. from the normal the test may be disregarded as of no significance. The diastase reaction is therefore practically limited to pathological conditions of the pancreas or to closely allied diseases. A very full list of references is appended. C. G. L. W.

Richards, A. N. Kidney function. *Am. J. Med. Sci.*, 1922, **163**, 1.

A review of the filtration theory of kidney function with a *résumé* of the results of the author's application of Krogh's method of microscopical examination of the capillary blood-flow to the kidney of the frog. The action of various diuretics was studied in this manner and found to increase the number of visibly active glomeruli. The circulation of each capillary tuft is independent of its neighbours. The glomerular blood-flow is irregularly intermittent. O. L. V. de W.

Mayes, E. B., and **Watt, J. M. Renal blood-flow and glomerular filtration.** *J. Physiol.*, 1922, **56**, 120.

The authors employed Cushny and Lambic's method of estimating the blood-flow through the kidney: the proportion of plasma in the blood was estimated by the haematocrit, and the sulphate content of the plasma and urine were determined. It appeared that the glomerular filtrate amounted to about 25 per cent. of the whole plasma circulating through the kidney

but that wide variations occurred, the filtrate sometimes falling to 6 per cent., or rising to 40 per cent. These variations could not be definitely assigned to any of the physical factors studied, and it is suggested that the explanation lies in alterations in the permeability of the glomerular filtrate.
O. L. V. de W.

Mayrs, E. B. Relative excretion of urea and some other constituents of urine. *J. Physiol.*, 1922, **56**, 58.

The concentration of urea and SO_4 in the plasma (after injection of gum-sulphate solution) was estimated in rabbits, and compared with the corresponding concentrations in the urine. The sulphate was concentrated to a considerably greater extent than the urea. Phosphate is concentrated from plasma to urine to practically the same extent as sulphate, and the same appeared to hold for creatinin. The results for the latter substances suggest that the tubules absorb water containing these bodies in minimal amount rather than an identical specific secretory power of the kidney for each of these separate substances. Urea is assumed to be reabsorbed by the tubule to a considerable extent, and is looked upon as a substance of a low threshold value. A raised ureteric pressure increases the difference in concentration between urea and sulphate, the output of the former being reduced to a greater extent. O. L. V. de W.

Stepp, W., u. Feulgen, R. Acetaldehyd ein Bestandteil des normalen Harns. [**Acetaldehyde—a constituent of normal urine.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 72.

Acetaldehyde has been previously detected in diabetic urine and the present investigation shows that it is a constituent of normal urine, which contains about 0·3 mgm. per litre. H. W. D.

Fricke, R. Eine Untersuchung über das Vorkommen von Brenztraubensäure in normalem und Diabetikerharn. [**An examination of normal and diabetic urines for pyruvic acid.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 39.

A search for free pyruvic acid in normal and diabetic urines failed to give a positive result. The author considers, however, that this acid may, if present, react with some other urinary constituent and so escape detection.
H. W. D.

Linder, G. C. Excretion of potassium iodide in the urine in health and disease: its use as a test of renal function. *Quart. J. Med.*, 1922, **59**, 227.

The author has reinvestigated this method of testing the functional efficiency of the kidney. Two grammes of potassium iodide were given, and the iodine excretion estimated in the two succeeding twelve-hour periods. In 4 normals the excretion during the first twelve hours varied from 44 to 60 per cent. of the dose. He regards an excretion below 35 per cent. as a definite indication of impaired function, and a reduction to 15 per cent. as a sign of very advanced disease. O. L. V. de W.

Schumm, O. Über den Nachweis kleiner Mengen von Blei im Harn. [**The detection of small amounts of lead in urine.**] *Ztschr. f. physiol. Chem.*, 1922, **118**, 189.

The applicability of several methods for the detection of small amounts of lead in the urine in cases of lead poisoning is examined. The author finds the most satisfactory method to be that of Meillère, modified as follows: 15 c.cm. 25 per cent. HCl and 0·4 gm. $CuSO_4$ are added to $1\frac{1}{2}$ litres of urine. H_2S is then passed through the liquid, first at ordinary temperature and then at about 40°–50° C. The precipitate is collected, extracted with nitric acid, and the extract electrolysed at a tension of about 4 volts and a current strength of 0·5 amperes. An electrolytic separation of the copper and lead occurs, the latter metal depositing on the anode, an extract of which will give typical reactions of lead. The method serves to detect amounts of the order of 0·1 mgm. lead per litre. H. W. D.

Smith, Millard. **A micro modification of the method of Benedict for the quantitative determination of reducing sugar in urine.** *J. Lab. & Clin. M.*, 1922, **7**, 364.

A micro-method in which 1 c.cm. of the Benedict quantitative solution is used, and the titration conducted in a specially devised test-tube.
O. L. V. de W.

Rohonyi, H., u. Lax, H. Über Stickstoff-Retention und Rest-N-verteilung in den Geweben bei Niereninsufficienz. [**Nitrogen retention of non-protein nitrogen distribution in the tissues in renal inadequacy.**] *Ztschr. f. klin. Med.*, 1922, **92**, 217.

The nitrogen balance and the non-protein nitrogen content of the blood were studied in 4 cases of chronic nephritis for periods of 22 to 96 days. Large amounts of nitrogen were retained, without appreciable alteration of the non-protein nitrogen content of the blood: thus in one case with a total nitrogen retention of 200 gm. in 33 days, the non-protein nitrogen of the blood at the beginning and end of the period was found to be 40 mgm. per 100 c.cm. It is possible that the excess nitrogen is stored as protein. Tissues from patients who had died without renal lesions showed a non-protein nitrogen content 8 to 10 times as great as the blood. In patients dying of uraemia, the non-protein nitrogen content of the tissues was only slightly raised, and no increase was found in the protein nitrogen: the non-protein nitrogen of the blood was high and almost equalled that of the tissues. It is suggested that in the last stages of nephritis the tissues lose their 'nitrogen affinity' and a rapid rise results in the non-protein nitrogen of the blood.
O. L. V. de W.

Marsh, P. L., Newburgh, L. H., and **Holly, L. E.** **Nitrogen requirement for maintenance in diabetes mellitus.** *Arch. Int. Med.*, 1922, **29**, 97.

Protein metabolism above the minimal is undesirable in diabetes owing to the great glycogenic property, and specific dynamic action of protein. Nitrogenous equilibrium can be established in this disease according to the laws applicable to the normal subject, provided that the total caloric requirement of the subject can be satisfied. This implies that he must be able to burn enough glucose to metabolize fat. Diabetics who cannot burn this small amount are exceedingly rare. O. L. V. de W.

Fricke, R. Über die Auffindung von Aldol im Diabetikerharn. [**The discovery of aldol in diabetic urine.**] *Ztschr. f. physiol. Chem.*, 1922, **118**, 218.

A very small amount of aldol was detected in diabetic urine. This hydroxy-aldehyde probably has some significance, being possibly a connecting link between acetaldehyde and β-hydroxybutyric acid. H. W. D.

RADIOLOGY AND ELECTROLOGY

Radiotechnique

Rieder, W. Prophylaxie du mal des rayons. [**Precautionary measures against the harm done by X-rays.**] *J. de radiol. et d'électrol.*, 1921, **5**, 515.

The author has undertaken a series of inquiries into the causes of X-ray sickness, described in France by M. Béclère as 'the Sickness of Profound Irradiation', or, briefly, 'Radiation Sickness'. It is known that ray sickness manifests itself by the following symptoms: headache, feelings of nausea, vomiting, depression, lassitude, and even in certain cases a rise in temperature. The author takes the causes to be: toxic effects of the gas in the radiotherapeutic rooms, effects upon the cells of the body of electric discharges, the toxic effects of too powerful doses, and irradiation in the region of the viscera.

To avoid the trouble, or, at any rate, to reduce it to a minimum, the author recommends reducing the ozone to the smallest quantity; the prevention of sparking in the open air, the installation of high tension conductors (polished and without angles), operating in spacious and airy rooms. Apart from all this, he recommends tying down the patient in order not to expose him to an electric discharge. [We think it advisable formally to discourage this mode of action, as, in the event of the cable falling down, the patient would act as a conductor. It is far wiser to adopt the method of M. Béclère, who covers the patient entirely with a layer of metal.]

The author recommends limiting the application of the rays to the actual seat of trouble, and giving generous doses of laudanum-scopolamine. Sometimes a belated sickness, which has the appearance of being caused by absorption of tumour tissue makes its appearance some few days after the irradiation treatment. This is not attended by any inconvenience, and can neither be prevented nor treated. M. B. D.

Radiodiagnosis

Van Zwaluwenburg, J. G., and Grabfield, G. P. Apical pleuritis and its relationship to pulmonary tuberculosis. A statistical study of stereoscopic Roentgenograms of 366 consecutive adults' chests. *Am. Rev. Tuberc.*, 1921, **4**, 323–38.

Van Zwaluwenburg's and Grabfield's second contribution to the study of apical pleuritis in relation to pulmonary tuberculosis appears as a timely corrective to the general tendency to focus attention on the hilus and peri-

bronchial areas. They believe they have established a definite aetiological and chronological connexion between apical pleuritis and pulmonary tuberculosis, although they admit that this is not the only route of infection of the lungs by the tubercle bacillus. In fact, it is quite possible that the route of infection may be different in the adult to what it is in the child. At any rate, pleural shadows over the apices are very common in the adult, and by insensible gradations these shadows pass into those of frank pulmonary tuberculosis. Chronologically, the apical pleuritis precedes the pulmonary disease; the prevailing tendency is for the disease to spread to the opposite apex and to the underlying lung, and it is probable that infection reaches the pleurae through the cervical lymphatics. C. L.

Myers, J. A. Studies on the respiratory organs in health and disease. A comparison of vital capacity readings and X-ray findings in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1922, **5**, 884–95.

Myers has investigated the vital capacity of 101 persons definitely suffering from, or suspected of, pulmonary tuberculosis. Frequent fluoroscopic examinations were made, and stereoscopic skiagrams were taken, all the plates being taken by the same roentgenologist to secure uniformity. Myers concludes that in suspect cases the vital capacity test is of great diagnostic value, and if there is a reduction of more than 15 per cent. it is usually of clinical significance, particularly when cardiac disease and pulmonary disease other than tuberculosis can be eliminated. This test is of special value if it has been made at some earlier period when the person concerned was in good health, as the standard thus obtained is more reliable than that worked out by formulae. But in cases of peribronchial tuberculosis, X-ray examinations are usually necessary to diagnosis, since the lung capacity in many such cases is well within normal limits. A very small, severe lesion may reduce the lung capacity more than an extensive but comparatively inactive lesion, and the X-rays are, therefore, more valuable in showing the extent of the disease. Indeed, in some cases of fairly extensive fibrous and calcified tuberculosis the lung capacity is within normal limits. The most valuable function of the spirometer is the following of the course of the disease; as it comes under control, the vital capacity increases, whereas it decreases if the disease is extending. The spirometer measures the ability and power of the lungs to function, while the X-rays record the nature and extent of the disease. Neither test is infallible; both are very valuable. C. L.

Radiotherapy

Quick, D. Radium and X-ray in tumours of the hypophysis. [B.] *Arch. Ophth.*, 1920, **49**, 256.

The author points out that examination with the ophthalmoscope and X-rays is usually conclusive and that the latter is particularly useful when bony destruction is noted. The pathology of tumours of the hypophysis is shortly dealt with. A review of surgery on these types of cases and of the results follows, from which the author concludes that it is far from being the ideal form of treatment. The results of treatment by many radiologists are given; in every case there was some improvement in the symptoms by

using radium and X-rays either together or separately. The author then describes three cases that came under his personal notice and the procedure of treatment. Radium alone was used, and the author thinks that possibly this was a mistake. He points out that if the patient be suffering from coryza or any nasal infection there is danger of death from meningitis. Three points are put forward in favour of radiological treatment: (1) there is no operative mortality; (2) pressure symptoms respond much more promptly and more uniformly and without pain or inconvenience; (3) it offers hope of benefit to every type of case except perhaps simple cysts, whereas the scope of surgery is limited. Other reasons for employing radiotherapy are also dealt with, and the advantages and disadvantages of X-rays and radium are discussed. On the whole the author favours the application of radium after a submucous resection of the septum nasi and possibly the removal of a window from the floor of the sella turcica so as to expose the gland directly. P. L.-B.

Passow, A. Beitrag zur Bewertung und praktischen Anwendung der Lichtbehandlung bei tuberkulösen Augenerkrankungen. Teil I. Bewertung von Augenbestrahlungen. [**On the use of light therapy in tuberculous affections of the eye.**] *Strahlentherapie*, 1921, **12**, 441.

An article devoted to the means of treating tuberculous affections of the eye with ultra-violet radiation. The author lays great emphasis, for this kind of work, upon the need for an accurate method of measuring the ultra-violet radiation used. He used for this purpose the Furstenau-Aktinimeter, an instrument based upon the alteration of electrical resistance of selenium when exposed to these rays; the degree of change of this resistance is apparently capable of serving in a quantitative manner as a method of measurement.

There is no doubt that the usual source of ultra-violet radiation, namely, the mercury arc, does change in its yield of radiation for the same power supplied. This is generally attributed to a change in the opacity of the containing quartz vessel; such a variable makes it all the more necessary to have reliable measuring instruments of the yield of radiation.

The author prefers the use of ultra-violet radiation to radium and X-rays in the particular diseases he deals with, owing to the damaging effects which these latter may have upon the healthy tissues of the eye.
S. R.

Fischer, J. F. Röntgenterapi ved Morbus Basedowii. [**X-ray treatment in Graves's disease.**] *Ugesk. f. Læger.*, 1922, **84**, 345–62, 385–94.

This paper by the late Prof. Fischer, of Copenhagen, deals with 490 cases of Graves's disease given X-ray treatment in private or hospital practice. Several cases were *formes frustes* (Basedowoid), marked nervous symptoms and a certain degree of tachycardia being unassociated with definite signs of goitre. The results of X-ray treatment in this class were, as a rule, very satisfactory and lasting. The 231 private cases could be grouped in 3 numerically equal classes, including cases in which (1) the diagnosis was doubtful, (2) the disease was slight, and (3) the disease was moderately severe or severe. Among the 490 cases there were only 11 males, the average age was 30–45, the extremes being 24 and 63 years.

The duration of the disease before treatment was usually 6 months to 5 years. The results were far better for the private than for the hospital cases, and relapses were far more frequent in the latter class owing to the overwork and household worries to which this class was unavoidably prone. In more than four-fifths of the total, 'positive' results were obtained, i. e. there was either a complete disappearance of all the symptoms or definite improvement lasting for a considerable time. In the remaining fifth no harm was done, with the possible exception of one case. As a rule the class of case in which the X-rays were least effective was that in which there was little enlargement of the thyroid, the nervous symptoms were not very prominent, and the clinical picture was dominated by tachycardia.

It is difficult to compare operative with X-ray treatment, because the former is usually reserved for picked cases, whereas almost every patient samples X-ray treatment. In two-thirds of his cases Fischer obtained partial or complete disappearance of the goitre; in the remaining third there was no apparent change in the size of the thyroid, although the patients' general condition was much improved. Soft goitres were most amenable to treatment, and hard goitres usually became softer before they began slowly to diminish in size. One patient, who was given X-ray treatment first for tuberculous glands in the neck and later for a small goitre, developed myxoedema, which rapidly passed off under treatment with thyreoidin. The skin being peculiarly sensitive in Graves's disease, transitory erythema is a comparatively common sequel to X-ray treatment, and care must be exercised especially in cases of relapse which require protracted treatment. Permanent changes in the skin may develop suddenly and unexpectedly, without any premonitory erythema; in about 3 per cent. of Fischer's cases more or less prominent telangiectasis developed. Severe and prolonged hoarseness, with redness and swelling of the vocal cords, was provoked in two cases, in one of which it lasted several months. But the X-rays' reputation for creating adhesions about the thyroid, and thus rendering operative treatment at a later date difficult, is certainly undeserved. Fischer can also find no confirmation of the view that X-ray treatment of the ovaries in the subjects of Graves's disease is as effective as X-ray treatment of the thyroid itself. But he has found a definite relation between ovarian function and X-ray treatment of the thyroid, for this frequently induced amenorrhoea of a couple of months' duration in women whose menstruation had hitherto been quite regular.

Fischer's dosage is above the average: debilitated patients are given 3 H. units through a 3 or 4 mm. aluminium filter at intervals of a couple of days. Two fields on each side of the neck and a central field are treated, and if serious symptoms are provoked the intervals between the treatment are prolonged. If it is well tolerated, the dosage is raised to 8 or 10 H. units with the same filter. Less debilitated cases are at once given 8 to 10 H. units through a 3 to 4 mm. filter, and after an interval of 2 to 3 months the dosage is increased to 10 to 12 H. units through a 4 to 5 mm. filter. Should a relapse occur, the last-named dose is repeated at intervals of several months. Fischer has given still larger doses, but has reduced them on account of the sensitiveness of the skin. He emphasizes the importance of X-ray treatment early in the disease, and the fact that operative treatment is dangerous, whereas there is practically no risk with X-ray treatment.

C. L.

Darier, J. Modes de début des cancers de la peau et de la bouche. Comment éviter ces cancers. [**Variations of onset in cases of cancer of the skin and of the mouth. How to avoid these cancers.**] *J. de radiol. et d'électrol.*, 1922, **6**, 197.

A cancerous growth is, according to the author, in its infancy, a purely local affliction, the appearance of which does not necessarily indicate in the patient an antecedent predisposition to cancerous disease. Once removed (in its very early stage) the patient may be said to be cured, and there need be no fear of any so-called predisposition causing an outbreak of the disease elsewhere. Nothing less than an histological examination can lead to a definite diagnosis of any one of the various kinds of skin epitheliomata.

1. **Spino-cellular epithelioma.** Treatment: immediate and radical surgical excision. The use of X-rays and radium to be strongly discouraged, seeing that such treatments are practically inoperative and even harmful in all cases, however early, of spino-cellular epitheliomata. The author qualifies these statements, however, by saying that recent experiments have shown that the use of powerful, cautiously selected rays *can* effectively combat this form of cancer.

2. **Baso-cellular epithelioma.** A remarkably slow development and a total absence of metastatic tendencies characterize this form of cancer. Moreover, it does not necessarily cause congestion of the glands. The accepted treatment is radiotherapy (ampoule or radium).

A variant of this type, i. e. mixed epithelioma, or Malpighian metatypic epithelioma, which can and does cause metastases and glandular involvement, is insusceptible to radiotherapeutic treatment, and calls for immediate and total excision (bistoury).

3. **Naevo-cellular epithelioma and cancer.** The accepted treatment is electrolysis.

Cancers of the mouth are, in most cases, of spino-cellular origin, and nine times out of ten they develop upon a basis of syphilitic leucoplakia.

It is, therefore, on these premises that the early cases must be searched for. Immediate surgical removal is imperative. Baso-cellular epitheliomata sometimes occur on the floor of the mouth.

The above are the author's directions for treating the various types of epitheliomata. It is advisable to go cautiously in X-ray and radium treatment, for, although of great value in cases of baso-cellular epitheliomata, X-ray and radium therapy are ineffectual, nay, even frankly harmful, in other cases. The author's opinion, although reliable and sound on most points, would appear to be, nevertheless, a trifle arbitrary regarding cases of spino-cellular epitheliomata.

The progress made in the technique of Curie therapy and Röntgen therapy doubtless permits of many cases being temporarily arrested and even apparently completely cured. Nevertheless, time alone will show us whether these fairly recent cures are lasting and complete. M. B. D.

Radiobiology

Warren, S. L., and **Whipple, G. H.** (1). **Roentgen-ray intoxication. I. Unit dose over thorax negative—over abdomen lethal. Epithelium of small intestine sensitive to X-rays.** *J. Exper. M.*, 1922, **35**, 187.

Warren, S. L., and **Whipple, G. H.** (2). **Roentgen-ray intoxication. II. A study of the sequence of clinical, anatomical, and histological changes following a unit dose of X-rays.** *J. Exper. M.*, 1922, **35**, 203.

Warren, S. L., and **Whipple, G. H.** (3). **Roentgen-ray intoxication. III. Speed of autolysis of various body-tissues after lethal X-ray exposures. The remarkable disturbance in the epithelium of the small intestine.** *J. Exper. M.*, 1922, **35**, 213.

I. The papers are part of the general study of 'non-specific intoxications', and deal with the systemic intoxication which develops after a suitable exposure to large doses of hard X-rays. The intoxication closely resembles that of intestinal obstruction. The authors believe that their experiments show that the fundamental point is a primary injury of the epithelium of the small intestine. For a normal 30–40 lb. dog the minimum lethal dose over the abdomen is 350 milliampere minutes; this has no effect if given over the thorax with the abdomen shielded. The outstanding abnormalities of the former are the necroses in the small intestine: large areas may show complete necrosis and disappearance of epithelium over the villi and lining the crypts; the inflammatory reaction is not so intense as would be expected. The lines on which the experiments were carried out are described fully. The results agree fully and show that enormous doses of X-rays may be given over the thorax without causing any clinical reaction in a normal dog; 300–512 milliampere minutes have been given. There is usually a slight transient leucopenia and may be a very slight rise in the total nitrogen excretion. After 2–3 weeks the hair drops out and the skin shows pigmentation; the ribs show loss of bone-marrow. The complete experiment on one dog is given in full; the clinical reaction from an exposure over the abdomen is remarkably constant. The intoxication is seen first two days after irradiation. Post-mortem findings are described in full; the small intestine is affected most and the colon to a lesser degree. Histologically the mesenteric glands are slightly haemorrhagic and contain pigment; spleen atrophic and contains pigment; in the ovary the ova are apparently dead. In the small intestine there is intense destruction of the epithelium, particularly in the ileum, where there are strenuous attempts at regeneration; this is less marked in the jejunum. The colon shows mucoid degeneration and slight necrosis of the tips of a few villi, with some evidence of repair. Experiments on three other dogs are also described. In the beginning of the discussion the authors lay stress on the fact that they used normal dogs and that therefore the experiments are probably less complicated than is the case in radiation of a diseased human being. They claim that they can rule out the red marrow as being a factor in the disturbances noted, and also lymphatic tissue. It is concluded that the circulating blood is little affected as a large part of it must be included in the thorax irradiations. As regards the abdomen, the kidneys are only slightly affected, the liver not at all, nor pancreas, nor adrenals: in the gastro-intestinal tract the small intestine is far the most sensitive, and the authors believe that injury to the epithelium of this part is the prime cause

of the intoxication and lethal poisoning. Death occurs almost always on the fourth day.

II. This paper supplements the foregoing. The macroscopic and microscopic changes in the epithelium of the small intestine are studied day by day. The urinary nitrogen shows a prompt rise on the day following the irradiation, and there are distinct histological abnormalities in the epithelium of the small intestine within the first 24 hours, although there is no clinical evidence of injury. The crypt epithelium suffers first; this, it is suggested, may indicate some difference between the epithelium of the crypts and that of the villi, which does not show much change till the third day. Five experiments, with the post-mortem and histological findings, are described fully. As a result of these the authors find that after a lethal dose of X-rays over the abdomen there is a remarkably uniform physiological reaction. In the first 24 hours the findings are negative clinically and anatomically, but histologically there are changes in bone-marrow, spleen, lymph glands, and ovaries, and nuclear changes in the crypt epithelium of the small intestine. In the second 24 hours there are slight gastro-intestinal disturbances; necrosis of the crypt epithelium may be complete, that of the villi is practically intact. In the third 24 hours the gastro-intestinal symptoms are more marked and anatomically there are changes in the gastro-intestinal tract. The crypt and villous epithelium has almost entirely disappeared; there is some oedema and invasion of wandering cells. In the fourth 24 hours the intoxication is at its height and death usually occurs: anatomically and histologically the picture is that of the third day, except that there is more evidence of mitosis and repair on the part of the intestinal epithelium. The stomach is not affected, but the colon may be to a slight extent.

III. The paper shows that cell autolysis of the epithelium of the small intestine is profoundly modified by X-ray exposures. A series of autolysis experiments was carried out, using sections from organs of the dogs described in Paper II. The method of obtaining sections at varying periods after death is fully described. The sections are studied with regard to the effect of radiation of autolysis *in vitro*. Four graphs illustrate the results of the experiments. Certain cells such as fibroblasts, mature connective tissue cells, and some others appear not to be affected. In the normal intestine autolysis of the mucosa starts at the tips of the villi and progresses slowly to the crypts; in the irradiated animal the crypt epithelium autolyses more rapidly than that of the tip. The findings in the various organs of normal and irradiated animals is discussed fully under various headings. The experiments show that the spleen, liver, and pancreas of an irradiated animal show more rapid autolysis than those of a control animal: the kidney shows no such change. The stomach and colon are much more resistant than is the small intestine. In conclusion, the authors say that they are not prepared to say what may be the significance of this disturbance of cell ferments in the intestinal mucosa. P. L.-B.

Schmidt, E. A. Experimentelle und histologische Untersuchungen über den Einfluss der Röntgenstrahlen auf die vitale Färbbarkeit der Gewebe. [**Experimental and histological investigations upon the effect of X-rays upon *intra-vitam* staining of tissues.**] [**B.**] *Strahlentherapie*, 1921, **12**, 517.

A long paper with two pages of bibliography, the latter largely the literature on intra-vitam staining.

The author seeks to show whether the action of these stains upon animal tissues is modified by subsequent irradiation by X-rays of the tissues. The method of experiment consisted of infecting a number of animals, guinea-pigs and white mice, with the stain (trypan-blue), dividing them into two lots, one being kept as controls while the other received a dose of X-rays throughout the body. After suitable intervals the animals in the two series were killed and the chief organs examined to see whether differences could be observed between the irradiated and non-irradiated tissues in so far as the action of the stain was concerned.

In many cases this proved to be the case, some illustrations bearing out the finding. The author's chief interest, however, was to see whether this action could be shown in tissues which ordinarily do not show any marked changes under irradiation when examined with the more usual methods of staining; this proved to be the case in several of the tissues examined.

The conclusions arrived at by the author are to some extent bound up with opinions as to the significance to be attached to changes in degree of the cells' capacity to stain with these intra-vitam stains, and it is therefore necessary to have some knowledge of these processes before the conclusions of the author can be critically valued. From his observations he concludes that there is ample evidence of the stimulating action of X-rays when applied in suitably small doses: there is of course already ample evidence of their destructive action. The communication comes from the Samariterhaus, Heidelberg. S. R.

Electrodiagnosis.

Société française d'électrothérapie et de radiologie médicale. (Proceedings.) [**The French Society of Electrotherapy and Medical Radiology.**] *Arch. d'électric. méd.*, 1921, **29**, 276.

Strohl spoke on 'the measure of electric excitability by means of the égersimètre'. A short description of the instrument is given. In experiments on the frog and healthy man his results as regards chronaxy were the same as those of other workers using other methods, but he had not obtained such large variations between the different muscle groups in healthy man as had Bourguignon. The latter thought that the greatest time employed should be lengthened for very degenerated muscles.

Bourguignon read a paper entitled 'Chronaxy and neuro-muscular Wallerian degeneration'. I. At first the contraction is brisk and the chronaxy varies between the normal and ten times normal, in the second stage it varies from 10 to 20 times the normal, and muscular relaxation is slower; in the third stage galvanotonus sets in suddenly and chronaxy varies between twenty times the normal and 0·009 secs.; in the fourth stage galvanotonus commencing suddenly occurs and chronaxy varies between 0·009 secs. and 0·02 secs., and lately between 0·015 secs. and 0·07 secs. II. In some cases there is a preliminary stage in which there is a temporary diminution of the chronaxy. III. The classical distinction between partial and complete R.D. is bad for reasons stated. Muscles in partial R.D. have two chronaxies, those in complete R.D. have only one. IV. These conclusions can be extended to the myopathies and Thomsen's disease. V. The term 'reaction of degeneration' is bad: in its early stages there is nothing pathognomonic. Diagnosis can only be established by conjoining electrical and clinical examination. P. L.-B.

Electrotherapy.

Zimmern, A. Electrotherapy in gynaecology. *Arch. Radiol. & Electrotherap.*, 1922, **26**, 301.

The author states that although electricity is little used at the present time, particularly since the war, the general results of its use sanction its usage. In some cases of fibroids, the uterine galvanic sound has been known to control haemorrhages which could not be stopped by radium or X-rays: 30–90 milliamps (positive pole) for five minutes twice a week is sometimes able to reduce or remove the haemorrhage. Successful treatment largely depends on correct diagnosis. In cases of metritis there are four methods of treatment: (1) galvanic current with positive pole introduced in the uterus, (2) the same with negative pole introduced, (3) ionic electrolysis, (4) high frequency. Positive cauterization is generally preferred when there is meno- or metro-rrhagia. Carbon sounds are used and should be introduced as far as possible and be of large size: a current of more than 40 milliamps should be used, particularly if fungosities or ulcerations are to be cauterized. Smaller currents should be used to begin with; in each case treatment depends on the patient and should not be followed by pain. Results may be obtained from the first seance, but usually five to fifteen are necessary. Obstinate haemorrhage, which either is not benefited or is made worse by treatment, is probably due to a submucous fibroid or a polypus.

If haemorrhage be not the most marked symptom and the metritis be of the dystrophic type, remarkable effects may be obtained from negative galvanocaustic treatment with 15–30 milliamps. By this method a hypersecretion is produced which drains the glands from within outwards. The high-frequency current seems to produce a similar hypersecretion. In cases of long-standing gonococcal metritis silver ionization is of great use; this may be carried out with a silver sound connected with the positive pole. Two seances a week with 20 milliamps for 5–10 minutes is sufficient, and in favourable cases after three to four weeks the patient becomes convalescent. Before extracting the sound the current must be reversed and a lower intensity used for one or two minutes. In all cases an acute, subacute, or purulent inflammation of the uterine appendages contraindicates electrical treatment. A short account is given of the author's method of treating dysmenorrhoea due to excessive flexion of the uterus. As regards stricture of the cervix, the author states that the same principles as those used in the electrolytic enlargement of the male urethra can be used both in congenital and acquired cases and that the treatment is without any danger: the technique is described fully.

In amenorrhoea and sterility negative electrolysis is also valuable. As regards the former, intra-uterine or intracervical applications with a galvanic current of 20 milliamps for five minutes two or three times in the week preceding the period may produce a favourable result. As regards the latter, the cause, in the author's opinion, is due for the most part to flexion or stricture, both of which have been referred to above; if salpingitis exists, galvanic current must not be used. If the cause be only congestion of the tubes, daily applications of the faradic current may be made.

In conclusion, the author refers to various other conditions in which electrotherapy may be of use, especially in cases of anal fissure. P.L.-B.

MEDICAL SCIENCE

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Biochemistry . . .	C. G. L. WOLF, M.D.

All communications on editorial matters should be addressed to

E. SCHUSTER, D.Sc.,

Assistant Secretary, Medical Research Council,

National Institute for Medical Research,

Hampstead, N.W. 3.

NOTICE.

In the references the letter [*B*] *after the title signifies that the original memoir contains a good bibliography of the subject dealt with.*

REVIEWS

SCARLET FEVER

Aetiology. G. F. and G. H. Dick, of Chicago, undertook experimental inoculation of volunteers (healthy men and women, aged between 18 and 35, who had not had scarlet fever) with subcutaneous injections of the blood-serum of patients in an early stage of the disease, citrated whole blood, gargling with filtered mucus from scarlet fever throats, subcutaneous injection of the same material, and swabbing the throats with pure cultures of haemolytic streptococci and also of a pleomorphic organism isolated from the throat in the early stage. No instance of scarlet fever was produced in any case. It would seem that the negative results reported following subcutaneous inoculation of blood-serum, whole blood, and filtered throat mucus are more conclusive than the negative results following throat inoculation.

Takahashi, of Tokio, injected five of his own children, aged between 3 and 10 years, subcutaneously with 0·0001 c.cm. of the blood of a scarlet fever patient. Not only did no general or local reaction ensue, but a certain degree of active immunity was produced, as was shown by the fact that hypodermic injection of 0·15 cm. of a scarlatinal patient's blood 50 days after inoculation, and smearing the child's throat with the secretions of the throat and blood of the patient 15 days after inoculation, failed to reproduce the disease.

Epidemiology. Kisskalt, of the Kiel University Institute of Hygiene, states that in Prussia, during the years 1901–12 the deaths per 10,000 inhabitants from diphtheria were 3·13, from whooping-cough 2·96, from scarlet fever 2·28, and from measles 2·17. The number of deaths from measles was often greater than that from scarlet fever, owing to the fact that many more children contract measles. In adults, unlike children, in whom the disease shows a preference for boys, the incidence is much higher in women than in men, sometimes twice as high. This is particularly true of the age-period 20 to 30. Attendance on the sick is no doubt a cause of this, but a special predisposition of the female sex, especially during menstruation, is also partly responsible. Kisskalt gives a table showing the annual mortality from scarlet fever in Berlin per 10,000 inhabitants since 1861, from which it is seen that the epidemics of the sixties, seventies, and eighties were attended with a very high mortality, e.g. 9·7 in 1865, 7·3 in 1875, and 7·9 per 10,000 inhabitants in 1881. Since 1885 the mortality from scarlet fever has shown a decline not only in Berlin but throughout Prussia, Baden, Saxony, Würtemberg and somewhat earlier in Bavaria. It is interesting to note that the scarlet fever mortality at Königsberg for the years 1773 to 1803 was 2·8 per 10,000 inhabitants, or just about the same as to-day.

Nielsen has investigated the incidence of scarlatina in Denmark since 1877, and has come to the conclusion that the decline in the frequency of this disease is slight and even doubtful. Children under 5 develop scarlatina less frequently, owing to the more effective isolation of cases occurring among

school children, and this decreased morbidity in the first five years of life accounts for the decrease in the mortality from scarlatina at all ages. A comparison of the incidence of scarlatina in Copenhagen, provincial towns, and country districts showed that it is directly proportional to the density of population. The mortality was about 14 per cent. in the first year of life, 4·5 per cent. in the period 1–5, and only 2 per cent. after the fifth year. The morbidity traced from one 5-year period to another showed a steady fall among children under 5, and a corresponding rise among children between 5 and 15.

Above the age of 15 there has been no change in the morbidity. It was noted that, in epidemics, the older children were usually the first to fall ill, and that the epidemic had not culminated among the younger children before a decline was demonstrable among the older children. Only towards the end of an epidemic would an appreciable number of children under 5 fall ill. In each age-period there was no change in the mortality, and the slight decrease of mortality for all ages seemed to be due entirely to the decrease of morbidity in the first five years of life. The incidence of the disease was least in the summer, greatest in the autumn or winter, but the months in which the minimum and maximum incidence occurred differed from year to year. The curves of epidemics showed abrupt rises and slow declines, and the frequency of cases under the age of 5 was comparatively greatest in the spring months, while in the autumn months comparative preference was shown for the age-period 5–15.

According to Newman, chief medical officer of the Ministry of Health, scarlet fever prevailed more extensively in England and Wales in 1920 than in any year since 1915 (119,490 cases and 1,430 deaths), but the increase was not uniformly distributed, the rate being far higher in London and in the principality of Wales than in any other territorial district. The actual number of cases notified in London during 1920 was 12,953.

Symptomatology. Bloch, of Coblenz, records a case of *surgical scarlet fever* in an infant, aged 18 months, due to sucking its thumb, as the result of which a gaping wound had developed. The case fulfilled the conditions required by Hoffa in 1887 for the diagnosis of surgical scarlet fever, viz. development of the eruption at the site of the wound after the appearance of lymphangitis, swelling of the tonsils and submaxillary glands, and typical desquamation. Bloch maintains that it is the duty of the practitioner to warn the parents of the danger of infection in the case of every wound, even a trivial breach of surface, caused by sucking, as scarlet fever is as likely to arise from this source as from the consumption of unboiled milk.

According to Hutinel and Nadal *relapses* in scarlet fever are more frequent in some epidemics than others. Marfan and Apert, among 256 patients, and Gouget among 858 cases, did not observe a single example. On the other hand Richardière and Kaufmann met with five cases of relapse among 522 patients. (From 1908–18 the annual incidence of relapse of scarlet fever in the Metropolitan Asylums Board fever hospitals has ranged from 1·28 to 3·02 per cent.—J. D. R.) Hutinel and Nadal attach considerable importance in the production of relapses to the coexistence in the early stage of scarlet fever of some more or less severe infection, the effect of this association being to modify the process of immunization. They record 10 cases of relapse in cases of scarlet fever associated with some other infection, viz. lobar pneumonia in 3 cases, acute articular rheumatism in 1 case, and various surgical infections in 6 cases.

In an article on *scarlet fever in the new-born* Dorner (1) records three cases to show that women suffering from scarlet fever may be safely allowed to suckle their infants, as infants during the first months of life are either entirely immune, or, if they contract the disease, the attack is so mild that it can only be detected on close examination.

Rosenbaum states that, from 1913 to 1919, 1,770 scarlet fever patients were treated at the Durand Hospital, Chicago, and 106 of them had *cardiac complications*, which in 94 developed in hospital and in 12 were instances of old heart disease. 88 of the 106 patients, or 5 per cent. of all the cases, had myocardial complications. 53 of them were mild, 30 moderately severe, and 5 very severe. Myocarditis might occur at any period of the disease, but was commonest in the later part of the acute stage or in early convalescence. Other complications seemed to increase the incidence of myocarditis. It was observed most frequently in the early years of life. Pericarditis was present in three cases or 0·17 per cent., of whom two died. Endocarditis was present in four cases or 0·22 per cent. Systolic murmurs at the apex were frequently present, but were usually regarded as functional or relative. The low percentage of endocarditis in Rosenbaum's patients as compared with the percentage of several other observers is attributed by him to the milder type of scarlet fever, in which the case mortality was less than 4 per cent. Unless it is very severe Rosenbaum does not think that old heart disease necessarily indicates a very serious prognosis in scarlet fever.

Hirsch, of the Department for Infectious Diseases of the Rudolf Virchow Hospital, Berlin, remarks that the condition of the heart and circulatory system in scarlet fever is of great importance, although the severity of the case is no guide as to the development of subsequent cardiac symptoms. The cause of severe and fatal cases is to be found according to Hirsch in acute lesions of the endocardium and myocardium combined with relaxation of tone and vasomotor paralysis. He mentions that scarlet fever, like every other infectious disease, may cause a true endocarditis in the second to third week of the disease and that cardiac complications, probably due to a mixed streptococcal infection, are not so rare as is asserted by Jochmann and Pospischill and Weiss (vide also *Medical Science*, 1920, **2**, 516–17).

A relatively large proportion of cases of the rare condition known as *purpura fulminans* have followed scarlet fever, as is shown by the fact that in 1910 Rolleston and McCririck collected 16 cases of this kind, and since then McConnell and Weaver, of the City Hospital, Cleveland, have collected seven more cases of this sequela of scarlet fever, including one of their own in a girl, aged 6 years, whose history was as follows: On the fifteenth day after the onset of scarlet fever and the seventh or eighth day of normal temperature, the temperature rose to 104° F. and the left foot became discoloured. Ecchymoses appeared on the body in the course of 48 hours, the urine and stools became bloody, and on the fourth day after appearance of the first ecchymosis death took place. In addition to the skin ecchymoses the autopsy revealed haemorrhages in the bladder, intestine, and brain. Microscopical examination showed that the discoloration was not due to gangrene but to interstitial haemorrhage following infectious thrombosis.

Dunham, of New Haven, Connecticut, has collected ten cases of *peritonitis* complicating scarlet fever from the literature from 1900 to 1919

inclusive, as well as a personal case in a girl, aged 5 years, who recovered after operation. In two cases the peritonitis developed in the eruptive period, one being fatal; in two cases in the desquamation period, one being fatal; and in the rest the time of onset was not stated. The diagnosis was confirmed by operation or at necropsy in four cases. In two cases a streptococcus was grown from the pus. Blood cultures were not reported in any of the cases.

Bungart records the case of a man, aged 31, who on the twenty-seventh day of a typical attack of scarlet fever developed *cerebral symptoms* characterized by headache and insomnia, on the forty-second day by aphasia, and five days later by the status epilepticus. Trephining was performed without an anaesthetic twelve hours after the first convulsive attack, and rapid recovery took place. The portion of brain substance which was removed from the left temporal lobe showed an inflammatory area of cerebral softening. Disease of the ear was excluded by otological examination, so that the infection must have taken place by the blood.

Barthe, who devotes his Paris thesis to the study of *miliaria* in the course of scarlet fever in children, states that it was first described by Stork, of Vienna, in 1759, and later by Zulatti, in 1763, from his experience of an epidemic in the island of Cephalonia. Miliaria in scarlet fever is rare below the age of three years and is infrequent in adult life, except in the puerperium. It has no effect upon the general condition, but its presence at the onset of scarlet fever may be regarded as an indication of an intense rash which will take a long time to disappear. Owing to its frequency at the onset of scarlet fever in children it possesses a real diagnostic value, and in the presence of a doubtful eruption should be regarded as evidence in favour of scarlet fever. Barthe maintains that it is important to be familiar with the desquamation following miliaria, so as not to confuse it with the true desquamation of scarlet fever, which it often closely resembles, and to avoid concluding that the case is one of erythema scarlatiniforme recidivans and thus overlooking the existence of scarlet fever.

Medi, of the Paediatric Clinic of Rome University, who records a case of suppurative *orchitis* in a child, aged $2\frac{1}{2}$ years, which developed on the eighth day of disease, remarks that only three previous cases of genital complications in scarlet fever have been published, viz. one by Henoch, in which inflammation of the epididymis and tunica vaginalis occurred on the nineteenth day of disease, a similar case described by Horteloup, and another reported at the Paediatric Congress at Montevideo in 1918 by Aucuña, of a child aged 9 years, who developed slight bilateral orchitis with inflammation of the tunica vaginalis on the eighth day of disease. Unlike Medi's case, none of these ended in suppuration.

Scarlet fever and tuberculosis. Kourtovitch, in her Paris thesis, states that there is no antagonism between scarlet fever and tuberculosis, and that the two diseases, as a rule, run their course independently without having any influence upon each other. There may, however, be a recrudescence of tuberculous lesions as the effect of a severe attack of scarlet fever, and when tuberculosis has reached an advanced stage even a mild attack of scarlet fever may cause a generalization of tuberculosis. Tuberculous lesions elsewhere than in the respiratory tract and cold abscesses with a fistula present an inflammatory reaction after the onset of scarlet fever, and in some cases fresh fistulae may form.

Diagnosis. The diagnostic test introduced by Schultz and Charlton

and known in Germany as the 'extinction sign' (*Auslöschphänomen*), of which a description was given in a previous issue (vide *Medical Science*, 1920, **2**, 520–1), has formed the subject of numerous recent papers not only in Germany (Dorner (2), Haselhorst, Meyer-Estorf, Steinkopf, Wöhlisch and von Mikulicz-Radecki) but also in Italy (Tron) and Switzerland (Reymond). While the observations of Dorner, Meyer-Estorf, Steinkopf, and Wöhlisch and von Mikulicz-Radecki confirm the value of the test, Tron, of the Milan Hospital for Contagious Diseases, and Haselhorst, of the Hamburg University Medical Clinic, are of a different opinion. Tron, who investigated the test in 50 cases of scarlet fever in which he performed 99 tests, comes to the conclusion that, though the sign does exist, its frequency is far from reaching a sufficiently high percentage to justify its being regarded as of diagnostic value, a positive result being obtained in only 10 out of 47 cases of scarlet fever. Haselhorst, who employed the test in 50 undoubted cases of scarlet fever and 13 other diseases, found that though it was not positive in any of the non-scarlatinal cases it was negative in as much as 20 per cent. of the cases in which the clinical diagnosis of scarlet fever was certain. The test usually failed to be of help in the doubtful cases with slight fever, atypical throat, and ill-marked and transient rash.

Friedemann, who is director of the Department for Infectious Diseases of the Rudolf-Virchow Hospital, Berlin, attaches considerable diagnostic importance to Widal's haemoclasic crisis, which he has hitherto found positive in all cases of scarlet fever, sometimes from the first day of disease and lasting well into convalescence. With few exceptions he has found the test negative in other infectious diseases. It is carried out as follows: The patient takes his last meal at 9 p.m., and at 8 a.m. on the following morning drinks 200 c.cm. of milk. The leucocytes are counted before and after the milk has been taken at intervals of 20 minutes. A fall of 2,000 is generally regarded as a positive reaction, but it is usually much more pronounced in scarlet fever.

Treatment. Weaver reports his observations on 54 cases of scarlet fever treated with immune human serum. All the cases were severe, 38 being of the toxic type, 6 being characterized by septic complications, and 10 showing a combination of toxic symptoms and septic complications. Only 2 deaths occurred, one belonging to the toxic and the other to the septic group. In neither case was any appreciable benefit derived from the serum. The blood was taken during the fourth or early in the fifth week of the disease, only those being chosen as donors who were free from any suspicion of tuberculosis, whose blood gave a negative Wassermann reaction, and who had had a typical attack of scarlet fever without complications. 200–300 c.cm. were taken from adults and proportionately less from bigger children. After the serum had separated from the clot, it was drawn off, mixed with serum from two or three other patients, and 0·3 per cent. of tricresol added. Cultures were made from the mixture, which, if it proved sterile, was placed in a small bottle of 30 c.cm. capacity and kept in a refrigerator until it was needed. The serum was injected intramuscularly in doses of 60–90 c.cm., half the amount often being injected into each thigh. Intravenous injections were occasionally used, but did not present any advantages. If no obvious improvement occurred or there was a tendency to relapse, a second dose was given after twenty-four hours. Beneficial effects following the injections occurred with great uniformity. Improvement in the general condition out of proportion to changes in the

temperature curve was the most striking phenomenon. Two or three hours after the injection the temperature began to decline, the fever sometimes terminating by crisis. In the absence of convalescent serum normal blood serum may be used.

Mironesco and Sager, of Bucharest, employed intramuscular injections of the serum of convalescents in 21 severe cases of scarlet fever. With the exception of five, aged from 9 to 18 years, all the patients were adults. They found that as a rule a single injection of 25–30 c.cm. of serum was sufficient to produce within 24 hours a fall in the temperature of two degrees and an improvement in the pulse and general condition. In only six cases was a second or third injection required. Of the 21 cases, three died, one, an adult, on the day after admission, and the other two, children, two days after admission, who showed miliary tuberculosis of the lungs and liver at the autopsy.

Cohn, assistant at the Infectious Department of the Barmbeck General Hospital, records a fatal case of scarlet fever in a woman, aged 24, following intravenous injection of convalescent serum. The autopsy showed evidence of septicaemia and severe damage to the heart. He alludes to other fatal cases of scarlet fever reported by Rehder, Glaser, and Griesbach (vide *Medical Science*, 1920, **2**, 521–2) following the use of convalescent serum, and also to non-fatal cases of rigor and collapse reported by Rowe, Reiss and Jungmann, Moog and Schultz. The serum used in the present case was a mixture of serums obtained from six convalescents and was five months old. It had been used a fortnight previously with success in the treatment of several other patients.

In 1915, and again in 1920, Sörensen published papers dealing with the treatment of scarlatinal otitis. His material consisted of about 4,000 cases of scarlatina treated at the Blegdams Hospital in the period 1910–12. Of the 57 cases of periauricular phlegmon treated on conservative lines, not one terminated fatally; whereas of 8 patients treated by radical operation, 3 died. Of the patients in the first group, 22 were cured, 24 showed some slight lesion persisting, such as a fistula behind the ear or a discharge from the ear, and 6 showed persistence of a still severer degree of inflammation. Sörensen concluded that it is wiser to adopt expectant treatment in scarlatinal otitis than to perform a radical operation at the first sign of middle ear disease and involvement of the mastoid process.

This attitude is severely criticized by Salomonsen, an aural surgeon attached to the Blegdams Hospital. His material covers the period May 1, 1918–Dec. 31, 1920, in which 4,447 cases of scarlatina were discharged. Of these 432 (9·7 per cent.) showed ear disease which was unilateral in 297 and bilateral in 135 cases. Operations were performed on 58 of these cases; of the remainder, 326 were discharged as cured, 64 suffered from a discharge from the ear, and 37 showed perforation without discharge. The routine treatment adopted for acute otitis was instant paracentesis as soon as signs of retention occurred. This was followed up by instillation with hydrogen peroxide and careful irrigation with tepid water, and paracentesis was repeated when the first opening became closed. A radical operation was undertaken as soon as definite tenderness and infiltration of the mastoid were observed, or the temperature assumed an irregular course, a rise to between 38° C. and 39° C., with remissions to normal for a few days, being sufficient to indicate operative interference even when examination of the ear and mastoid process proved negative. A third indication

for opening up the mastoid process was persistence of a discharge from the ear for more than six to eight weeks.

Analysing the 58 radical operations performed on 50 patients, Salomonsen discards several as being calculated to confuse the issue; deaths from pericarditis and concomitant diphtheria could not be debited in fairness to the operation. There remained 45 patients, 32 of whom were discharged completely cured; 6 showed some defect of the tympanum, and 6 suffered from chronic suppuration. Salomonsen claims that these figures compare very favourably with Sörensen's, and that to withhold all surgical interference until middle ear and mastoid disease have come to the surface in the form of a periauricular abscess is to court disaster. He holds that periauricular phlegmon in scarlatina is always the result of a mastoiditis, and is an indictment of the medical attendant, who should never have allowed mastoiditis to reach this stage. An early radical operation under general anaesthesia is, in his opinion, a far more conservative measure than a subsequent series of incisions, probings, and scrapings of a periauricular abscess without general anaesthesia.

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J. D. R.
C. L.

ALIMENTARY DISEASES

Hirsch, of the Bellevue Hospital, New York, who reports two cases, states that up to July 1920 146 verified cases of **atresia of the oesophagus** had been recorded in infants. The commonest type is a blind sac, a lower sac opening into the trachea above the bifurcation; 103 out of 146, or 70 per cent., are of this type. Associated abnormalities of other parts of the body are common. The most favoured embryological explanation is failure of closure of the tracheo-oesophageal septum.

Oettinger and Caballero report four cases, in patients aged from 47 to 75, of **megaoesophagus,** or idiopathic dilatation of the oesophagus, the characteristic features of which are difficulty and sometimes pain in swallowing, regurgitation followed by relief, and a chronic course with more or less acute exacerbations due to oesophagitis caused by a prolonged stasis of food. The anatomical condition consists in an increase in the calibre of the oesophagus with or without hypertrophy of its walls. In addition to

an increase in width there is also an elongation of the organ (dolicho-oesophagus). After review of the various theories proposed to account for the condition, the writers adopt Bard's view that this dilatation of the oesophagus is a sort of malformation similar to the megacolon described by Hirschsprung.

Moutier records three cases in women of **acute oesophagitis** following the administration of an anaesthetic (ether alone in two cases and associated with nitrous oxide in the third). The condition was apparently produced in the initial stage when each violent inspiration was followed by deglutition of the irritating vapour. The toxic action of the vapour was shown by its causing obstruction of the general circulation and mediastinal congestion and its caustic action by direct injury to the mucous membrane. None of the patients vomited after the operation, or at least had repeated vomiting. The symptoms developed at the end of about twenty-four hours when the first attempt was made to feed the patient. There was little or no spontaneous pain, but any attempt at swallowing caused a violent pain at the lower part of the neck or on a level with the xiphoid cartilage. Dysphagia was accompanied by intense salivation and lacrimation. Sometimes there was a more or less haemorrhagic sputum. Sympathetic symptoms, such as mydriasis, tachycardia, and flushing of the face, were associated with the pneumogastric symptoms. The affection lasted a week, reaching its height on the fourth day. Treatment consisted in hypodermic injection of $\frac{1}{4}$ or $\frac{1}{2}$ mgm. atropine to combat the spasm and check the salivation, and a mixture containing bicarbonate of soda and carbonate of magnesia was given every two hours. Feeding was resumed very gradually with tapioca and milk puddings.

While examining a case of **carcinoma of the oesophagus**, Luger, of Vienna, noticed, on careful percussion, an area of dullness on either side of the vertebral column, which became more extensive as the disease progressed. This finding was confirmed by subsequent examination of other cases of carcinoma of the oesophagus, and Luger now records 13 illustrative cases of this disease, in which a bilateral symmetrical or asymmetrical area of dullness of varying degree was found on either side of the vertebral column corresponding to the position of the tumour. The dullness usually disappeared in the knee-elbow position, and sometimes when the patient bent forward. Luger points out that this percussion sign can hardly be regarded as of great diagnostic value, as carcinoma of the oesophagus can be detected easily by clinical and X-ray examination, and this sign makes its appearance relatively late. Further observations, however, are required to show whether the sign is present in cases of deep-seated tumours of the cardiac end which require to be distinguished from spastic conditions of the oesophagus.

Lyon, Bartle, and Ellison, of Philadelphia, have found that the fractional method of **gastric analysis**, first employed by Hayem in 1905 and revived by Rehfuss in 1914, is of the greatest practical value, especially in cases where repeated X-ray examinations cannot be obtained, because it gives a very accurate picture of the motility of the stomach as well as its secretory curve. It is also of value in following the progress of medical treatment and estimating the benefit derived from surgical interference. On the other hand, Chiasserini, of Rome, while admitting that the fractional method represents an advance on the ordinary method of a single examination after a test meal, did not obtain such definite results as Rehfuss and his

collaborators, probably through lack of the special tube employed by these investigators.

Musser, jun., of Philadelphia, made fractional gastric analyses upon many soldiers suffering from simple tachycardia, tachycardia from gas poisoning, and similar conditions, and found that in patients suffering from neuro-circulatory asthenia there was a very definite increase in the total acidity and free hydrochloric acid as compared with controls. This seemed to add further evidence to that already accumulated that these soldiers were suffering from a neurosis with which was probably associated a hyper-irritable vagus.

Einhorn (1) made a fractional examination of the duodenal contents in 40 cases of peptic ulcer to ascertain whether the function of the duodenum of neutralizing acid chyme remained unaltered in organic affections of the stomach and duodenum. The majority of cases—24 out of 40—showed a normal condition as regards the alkalinity of the duodenal contents, while 16 showed at times an acid state in the duodenum either in the fasting condition or at one time or another during the fractional examination.

In most cases of complete **linitis** the disease is fairly rapidly fatal as soon as the diagnosis has been firmly established. Enriquez and Gaston-Durand, however, report a case in a woman, aged 41, of spontaneous retrogression of complete linitis after the disease had lasted eleven years. Unlike other cases of linitis in which it tends to spread to the subperitoneal tissue, the process remained exclusively localized in the stomach. The patient's tuberculous history suggested the presence of an interstitial non-ulcerative infection, which gradually subsided in the body of the stomach, while it persisted in the pyloric region.

Gastric and duodenal ulcer. Strauss, of Berlin, refers to Heissen, who, in 296 cases of gastric or duodenal ulcer, found a family history in only 16, or barely 5·5 per cent., whereas Spiegel, among 121 cases of gastric ulcer, found a suggestive family history in 26 per cent. as compared with a frequency of 5·5 per cent. among persons with healthy stomachs. Strauss himself, in a large special military hospital for diseases of digestion and metabolism, found among 218 patients with gastric or duodenal ulcer 70 cases, or nearly one-third, with a history of gastric disease in the family. He therefore concludes that hereditary and familial factors play an important part in the pathogenosis of gastric and duodenal ulcer (*vide* also *Medical Science*, 1921, **4**, 5).

Discussing the relation of peptic ulcer to pulmonary tuberculosis Hegemann states that of 247 undoubted cases of peptic ulcer admitted to the Rostock Policlinic during the last three years only 21, or 8·5 per cent., had a history and evidence of tuberculosis, as compared with the 20 per cent. of French writers and 15·8 per cent. in Grote's statistics, while of 534 cases of pulmonary tuberculosis 16 or 2·9 per cent., had a history and evidence of peptic ulcer. These figures tally with the well-known fact that in peptic ulcer there is almost always hyperacidity, whereas in pulmonary tuberculosis there is a subacidity of the gastric juice.

Clauss made a complete psychical and somatic investigation of 100 patients with gastric ulcer, 71 of whom were men and 29 women, in order to determine how far nervous factors played a part in such cases. He classified the cases in three groups. In the first group, which consisted of 45 patients, general bodily weakness had existed since childhood. All the women in this group were late in reaching maturity. General nervous symptoms were

present in almost all the cases. Some patients, however, whose nervous system and mentality had been previously normal, first developed nervous symptoms in the course of their illness. The second group consisted of 37 patients who were healthy and vigorous persons, chiefly of the male sex, without any general or local nervous symptoms. The third group, which formed a transition between the other two, consisted of 18 patients, some of whom were vigorous persons without a trace of any nervous symptoms, but in whom there was a history of gastric trouble dating back to early life, while the others were weakly, excitable persons, mostly women, with all the signs of defective physical development, who first presented symptoms of gastric ulcer after their fortieth year. Clauss comes to the conclusion that in a certain number of cases a neurogenic origin of gastric ulcer was possible, while in others, who were mostly men, and in whom the disease developed later, nervous factors were not responsible. Many of those patients were arteriosclerotic subjects, in whom vascular changes might play a part in the production of the ulcer.

Eggleston reviews 500 cases of peptic ulcer which have been treated since 1912 at the Battle Creek Sanitarium, Michigan. 415 were classed as duodenal and 85 as gastric. More than 10 per cent. were penetrating ulcers which had burrowed through the posterior stomach-wall into the neighbouring organs or tissues, usually the liver or spleen. In 19 per cent. a history of haemorrhage was obtained. Of 156 cases which had been treated medically, and in which a period of at least three years had elapsed since the disappearance of their symptoms, 113, or 72 per cent., reported no return of symptoms, and 43, or 28 per cent., reported recurrences. In practically all cases a chemical study was made of the gastric contents. In 73 per cent. hyperchlorhydria was found, in 11 per cent. hypochlorhydria, 14 per cent. were normal, and in 2 per cent. there was achylia. The mortality was only 2·2 per cent. Eggleston comes to the conclusion that if peptic ulcer, particularly duodenal ulcer, is observed early in its history, and if the patient submits to a carefully planned course of treatment for a reasonable time and will follow up the treatment by a carefully regulated dietary regimen for some months, one may be sanguine of obtaining a complete cure. In uncomplicated, long-standing cases medical treatment afforded relief in at least 70 per cent.

Anders, of Philadelphia, describes a new sign of gastric ulcer, which consists in increased epigastric tenderness corresponding to the site of pain after food, when the patient is standing or sitting as compared with the dorsal decubitus. The sign is most marked in cases in which the ulcer is situated on the anterior wall of the stomach. The sign may also be present in cases of carcinoma situated on the anterior wall of the stomach, but is less marked than in ulcer.

Faber, professor of medicine in the University of Copenhagen, draws attention to the distinction as regards symptomatology and prognosis between ulceration in the juxta-pyloric region and that occurring in higher portions of the stomach. He shows that, while juxta-pyloric ulcer is more frequent in men, ulcer of the body of the stomach is more frequent in women. The symptoms of ulceration of the body of the stomach are comparatively insignificant, and a large number of such ulcers probably occur and heal without even being diagnosed.

Le Noir, Richet *fils*, and Jacquelin (1) examined the state of the hepatic and renal functions in 43 cases of active or cicatrized gastric ulcer and

found biological evidence of a slight degree of nephritis in 43 per cent. and of a pronounced degree in 25 per cent. On the other hand, clinical evidence of renal insufficiency was usually absent. In only one instance was there evidence of chloride retention. In most of the cases hepatic insufficiency was clinically latent, but the application of various tests, such as the production of glycosuria by administration of glucose, determination of the coagulation time, digestive haemoclasia, and the investigation of urobilinuria, showed that hepatic insufficiency was almost constant in the course of gastric ulcer, since in 23 cases in which this insufficiency was investigated one test at least was always positive, and often two or three. The writers suggest that certain clinical manifestations of gastric ulcer are not so much due to the ulcer itself as to the hepato-renal insufficiency complicating it. In the first place, although the haemorrhages in gastric ulcer are usually due to vascular ulceration, the writers have seen two cases, confirmed by autopsy, in which the haemorrhages appeared to be caused not by the gastric lesion but by a deficient coagulability of the blood due to impaired activity of the liver, which had undergone severe anatomical changes. Secondly, although the vomiting which occurs in gastric ulcer is generally caused by pyloric spasm or stenosis, gastric hypersecretion, or a special nervous condition of the patient, some cases are due to hepato-nephritis. Thirdly, gastric ulcer patients suffering from hepatic insufficiency are very slow in putting on fat, either before or after operation, in spite of rest in bed and superalimentation. Fourthly, post-mortem findings sometimes show that latent renal or hepatic lesions are responsible for the phenomena of shock which follow certain operations for gastric ulcer. The practical conclusions to be drawn from these facts concerning renal and hepatic insufficiency in gastric ulcer are, first, that considerable care must be taken in the administration of the sedatives usually recommended for the pain of gastric ulcer, such as preparations of opium, whereas, secondly, hepatic opotherapy, which stimulates the activity of the liver or causes relief of congestion, may be advisable in some cases. Thirdly, in the choice of an anaesthetic preference should be given to one that is not toxic for the liver, such as nitrous oxide, or local or spinal anaesthesia. Chloroform should be absolutely prohibited. Fourthly, in the presence of hepatonephritis, the operation should be limited to a gastro-enterostomy, gastrectomy or pylorectomy being performed later if the patient's condition allows it. Fifthly, the urine should be carefully examined during the post-operative stage.

Crohn, of New York, who records three illustrative cases, calls attention to the fact that a fully-developed gastric or duodenal ulcer may often be present simultaneously with the easily recognizable and familiar picture of tabes, although the discovery of characteristic signs of tabes may lead the practitioner to ignore the possibility of a coexistent abdominal lesion. The percentage of cases of tabes accompanied by gastric ulcer is difficult to estimate, as in general hospitals neurological cases as such are not admitted to the medical wards. Crohn has been unable to find in the literature any record of syphilitic ulcer or gumma of the stomach in a tabetic patient with gastric crises, and is of opinion that the ulcers found in tabes are probably simple peptic and not syphilitic ulcers or syphilis of the stomach. A case of coexistence of tabes and gastric ulcer is also reported by Shuman.

According to Cassanello, of Spezia, lead poisoning is probably a more frequent factor in the aetiology of duodenal ulcer than the small number of cases on record would lead one to suppose. As the elimination of lead takes

place by the alimentary canal and the liver, the duodenum is more exposed than the rest of the intestine to the deleterious effects of the metal. The carelessness of lead workers who do not wash their hands before meals, and their habit of keeping the type and brushes in their mouths, explain the readiness with which intoxication takes place. In three cases reported by Cassanello, the patients had been working in lead for 11, 10, and 3 years respectively, and had all shown undoubted signs of plumbism (colic, anaemia, cachexia, and constipation) before signs of duodenal ulcer developed (haematemesis, melaena, pain after food, &c.), followed by stenosis (constant vomiting, gastric dilatation, and emaciation).

Glaser, of Berlin, who found ulcers in the stomach and duodenum in a very large proportion of cases of plumbism, in no way differing from ordinary peptic ulcers, considers that the ulcers in such cases are not the results of a special predisposition, but are caused by toxic vagotonia.

According to Paterson, who records two personal cases in marasmic infants, aged 3 to 6 months respectively, with a review of the literature, duodenal ulcer is a rare condition in infancy, but would probably be found to be commoner than is at present admitted if a more careful examination of the duodenum were made in marasmic infants. Ulcers may be present in melaena neonatorum, and in older infants may follow on any gastro-intestinal upset. They may complicate extensive burns or septicaemia. In older children tuberculosis is the common cause. The diagnosis is extremely difficult, and is usually not made. Duodenal ulcer, however, should be suspected if there is a history of tarry stools or bright blood in a marasmic infant with previous gastro-intestinal upset after exclusion of colitis, intussusception, and polypus. Duodenal ulcer in infancy may be treated successfully by operation, as is shown by Palmer's case, in which gastro-enterostomy was performed at the age of $6\frac{1}{2}$ months.

According to Bosányi, of Budapest, who records two illustrative cases in infants aged $2\frac{1}{2}$ and $3\frac{1}{2}$ months respectively, in each of whom duodenal ulcer developed during erythrodermia desquamativa, extensive disease of the skin, even of infective origin, may be the direct cause of duodenal ulcer from the metabolic disturbances occurring in the skin rather than from the bacterial products. In both the present cases duodenal ulcer was regarded as a probable diagnosis during life owing to the occurrence of haematemesis and melaena in association with as extensive damage to the skin as occurs after burns, and the diagnosis was confirmed by the autopsy. Bosányi regards the causes of the ulceration in these cases to be as follows: (1) toxic products resulting from the disintegration of albumin which cause changes in the intestinal juices and glandular secretions; (2) auto-digestion as the result of increased tryptic activity of the pancreatic juice; (3) diminished resistance of the site of predilection for the ulcer in consequence of changes in the circulation.

Palefski, of New York, who summarizes the findings in 361 cases of duodenal ulcer and periduodenal adhesions, states that the duodenal tube offers the best means of visualizing the course of the entire duodenum. He regards a high acidity, blood in the duodenal contents, and a normal duodenal curve with the duodenal tube *in situ* as pathognomonic evidence of duodenal ulcer, and a normal or subnormal acidity, absence of blood in the duodenal contents, and a distorted duodenal curve as pathognomonic evidence of periduodenal adhesions, usually the result of gall-bladder infection.

Shattuck, of New York, studied the early effects of the Sippy treatment

on the symptoms, gastric chemistry, evidence of occult haemorrhage, and X-ray findings in 28 cases of peptic ulcer (6 gastric and 22 duodenal) over periods ranging from six months to two years. 22 of the 28 patients remained free from symptoms throughout the period of observation. Of 17 patients studied with the Ewald test meal or the fractional method, 10 showed no marked reduction in acidity, though all but 2 were rendered free from symptoms. Six of the 28 patients showed occult blood in the stools, which disappeared in all cases after three weeks. Five out of 7 patients with duodenal ulcer, who were followed from one to two years, showed evidence of favourable X-ray changes. In 5 out of 6 cases of ulcer of the lesser curvature the niche deformity and six-hour residue disappeared.

Galambos recommends the substitution of barium sulphate for bismuth subnitrate in the treatment of gastric and duodenal ulcer, as it possesses the following advantanges: complete insolubility, harmlessness, cheapness, and tastelessness. The action of barium sulphate generally resembles that of bismuth salt in forming a protective layer over the gastric or duodenal ulcer, as is proved by X-ray examination. The constipating action of barium sulphate, on the other hand, is less marked than that of the bismuth salt. Consequently barium sulphate leaves the gastro-intestinal canal more rapidly than bismuth. Another advantage of barium sulphate is that while the bismuth salt, owing to its conversion into bismuth sulphide, gives a greenish colour to the stools and thus interferes with the naked-eye recognition of occult haemorrhage, the white barium sulphate makes the haemorrhage in the stools more distinct.

During the last seven years Smithies, associate professor of medicine in the University of Illinois, has observed 76 instances of **cardiospasm**, i.e. unusually strong and prolonged contraction of the cardiac sphincter associated with diffuse dilatation of the oesophagus. Of 47 tabulated cases 25 were females and 22 males. The ages ranged from 19 to 70, the average age being 39·2. According to Smithies, the initial over-stimulation to the cardia is exerted by numerous factors which may be extra-oesophageal or intrinsically oesophageal. The stimuli may arise from the central nervous system, from the oesophagus itself, the diaphragm, the intrathoracic organs, the stomach, duodenum, gall-bladder, appendix, or other abdominal viscera. In some patients more than usually powerful contractions of the cardiac sphincter are initiated by psychical disturbance. In all but 17 of Smithies's cases the onset was acute. The duration of the symptoms averaged 5·6 years and ranged in individual cases from three months to twenty years. There was constant dysphagia in 45, dysphagia to fluids only in 21, to solids only in 14, and to both in 12. Dysphagia was almost always accompanied by vomiting or spasmodic regurgitation of food. The vomiting was usually sudden, frequently explosive, and very often occurred shortly after the ingestion of food. Loss of weight ranging from 10 to 82 lb. occurred in all the patients, the average loss being 29·2 lb. Normal bowel movements occurred in 47 per cent. In the remainder there was obstinate constipation. Smithies maintains that under proper treatment clinical and functional recovery takes place in 70 per cent., improvement in 20 per cent., and no benefit in 10 per cent.

According to Finney and Friedenwald, who record eleven illustrative cases, **pylorospasm** is a complex nervous phenomenon, the exact aetiology of which has not been satisfactorily settled. It may exist in one of three types: the neurotic, the irritative, and the reflex. In the largest percentage of

cases the condition is secondary to some irritative lesion in the stomach or is reflex from disease of some other organ. Many of the cases are promptly relieved by the removal of the cause, e.g. chronic appendix, gall-stones, &c. There exists, however, a purely neurotic form without any demonstrable lesion. The condition can usually be recognized clinically. The symptoms consist of pains of the hunger type appearing two or three hours after meals, which are relieved by emptying the stomach of its contents as well as by ingestion of food; of contractions of the stomach leading to tumour formation, which disappear as the spasm relaxes; of symptoms of intermittent stagnation and hyperacidity. Pylorospasm is best recognized by X-ray examination, by means of which the nervous as well as the organic forms may usually be differentiated. Treatment consists in overcoming the primary neurasthenia by dietetic or hygienic measures. During an attack the best results are obtained by hypodermic injections of morphia with atropine following a thorough lavage of the stomach. Atropine in full doses is the most useful drug. When medical treatment fails, pyloroplasty gives the best results.

Gastric cancer. Taylor and Miller have analysed 182 cases of cancer of the stomach admitted to the University of Pennsylvania Hospital with special reference to the incidence of pre-existing ulcer, their results being as follows: (1) A history of pre-existing ulcer was obtained in only 17 per cent. (2) The age incidence for the beginning of 'ulcer' symptoms in the ulcer-before-cancer cases showed that about one-third of the total number occurred in the fifth decade with as many in the sixth as in the fourth, in contrast with the acme of incidence of gastric ulcer, which occurs in the third decade. This suggests either that ulcers giving rise to symptoms in middle life are much more likely to become malignant than are ulcers generally, or that ulcer-before-cancer cases are really malignant from the beginning.

According to von Bomhard, who records an example in a woman aged 55, although a large number of reported cases cannot withstand criticism, it is an undoubted fact that carcinoma may develop in a chronic gastric ulcer. Such an event is relatively rare. Among 159 cases of gastric carcinoma Borst found only 9, or 5·6 per cent., in which carcinoma developed from an ulcer, while Konjetzny, at the Kiel Clinic, found only 1 among 98 cases. On the other hand Hammerschlag estimated the frequency at 19 per cent., Tiemen at 15 per cent., and Payr at 26 per cent. Von Bomhard maintains that the impossibility of distinguishing macroscopically a callous ulcer from gastric cancer should increase the indications for resection of a callous ulcer.

Mayo states that it will take years of observation to estimate fairly accurately the percentage of cancers which have developed a gastric ulcer, even if from 1 in 12 to 1 in 6 are thus developed. Personally he believes that the percentage is higher.

Laird, of Edinburgh, reports a case of columnar-celled carcinoma of the lesser curvature of the stomach in a boy aged 15, with extensive metastases in the gastric, pyloric, aortic, and mediastinal lymph glands, liver, pancreas, and diaphragm. Like the great majority of cases of gastric cancer under 30, the patient was a male. The other noticeable features in the case were the rapid course, death occurring only two months after the first symptom, temporary improvement after laparotomy, which the patient survived four weeks, and the rare metastatic involvement of the diaphragm.

Lilienthal, who records a case in a woman aged 26, states that since Mathieu's paper on gastric cancer in young persons, published in 1884, based

on 27 cases, and Gander's article in 1904, based on 46 cases, no reviews on this subject have appeared, although about sixteen isolated cases of gastric cancer in persons under 30 have been recorded in the literature of the last twenty years. In most of the cases of juvenile gastric cancer there is a characteristic clinical picture consisting of a sudden onset, rapid and febrile course, absence of cachexia, and early formation of metastases. As regards the gastric chemistry and motility, the presence of blood in the gastric contents and stools, the digestive symptoms, X-ray findings, and situation of the growth, gastric cancer in young persons does not differ from that occurring in later life. An early diagnosis is even more difficult than in older persons. The presence of a malignant growth is first indicated by signs of obstruction and a palpable tumour in the gastric region. Operation is usually too late to be of any help.

During the last two years Witthauer has seen four cases of gastric cancer among persons aged from 17 to 27 among the relatively small number of admissions to St. Elizabeth's Hospital at Halle. Three of those cases presented carcinomatous metastases at the umbilicus. During the same period another three cases of gastric cancer with umbilical metastases were observed in patients aged from 41–61. The fact that none of these patients was admitted with the correct diagnosis indicates how little is known of the occurrence and appearance of an umbilical metastasis, the diagnosis on admission in these cases being gastric catarrh or umbilical hernia. Witthauer urges that more attention should be paid to the umbilicus in a case suggestive of gastric cancer, so that an early diagnosis may be made and the patient given the benefit of an operation, the existence of an umbilical metastasis not forming a contra-indication thereto. Unlike Lilienthal, Witthauer found no characteristic symptoms connected with juvenile gastric cancer, such as sudden onset, rapid course, and absence of cachexia.

Willemse has recently seen two cases of gastric cancer with well-marked clubbed fingers. In one case the body of the stomach and in the other the pylorus was affected. The cause of the clubbing was obscure, as neither venous obstruction nor toxic factors were sufficient to explain it.

Van der Perk records a case of gastric cancer in a woman, aged 47, in whom the most prominent symptoms during life were fracture of the right clavicle and right sixth rib, and blood in the stools. There were no gastric symptoms. The autopsy showed carcinoma near the pylorus and metastases in the ovaries, right clavicle, pleura, and paravertebral tissue from the third to the sixth rib. No lesions were found in the liver, spleen, pancreas, intestine, appendix, mesentery, or uterus.

According to Le Noir, Richet *fils*, and Jacquelin (2), hepatic and renal insufficiency may occur in cancer of the stomach, but is less frequent and severe than in gastric ulcer. The only symptoms that may be attributed to this cause are a pronounced tendency to vomiting and haemorrhages and a terminal condition of delirium, coma, and operative shock. The hepatic lesions are slight and scanty even in the neighbourhood of secondary growths, while the renal lesions are most frequent but rarely intense. When gastric ulcer is associated with carcinoma, hepatic and renal insufficiency is more marked and is almost invariably present.

Van Lier, of Utrecht, states that there is too great a tendency to attribute symptoms in persons over 60 to the presence of cancer, especially in the cases of gastric disease. On the other hand, he maintains, first, that

the development of cancer in chronic gastric disease is rare in advanced life, secondly, that gastric ulcer rarely undergoes cancerous degeneration, and thirdly, that aggravation of long-standing gastric symptoms in old age is usually not due to cancer. During the last eighteen months he has observed no less than seven cases of benign gastric disease in persons aged from 68 to 82, who were almost all at first supposed to be suffering from cancer. All recovered, however, after gastro-enterostomy, at which hypertrophy of the pylorus or a true fibroma only was found. The distinguishing features from cancer in such cases were to be found chiefly in the history, the general appearance (except in neglected cases), the high acid values, and the high degree of retention.

Blumgarten emphazises the rôle of the thyroid and adrenal glands in **gastric neurosis** associated with disturbances in the gastric secretion, and classifies such cases into the following three groups: (1) Cases which show definite signs of a mild form of hyperthyroidism or thyroid deficiency. (2) Cases in which the gastric symptoms are the earliest manifestation of a hyperthyroidism or a hypothyroidism, which subsequently develops into the classical syndrome. (3) Cases which show the characteristics of the domination of the adrenals or of the thyroid.

According to Crohn and Reiss, of the Mount Sinai Hospital, New York, who made fractional tests on 50 cases, gastric hypersecretion is a functional disturbance of the secretory apparatus of the stomach and not a disease *per se*. It is a frequent symptom, occurring most commonly in males, and is present in probably 10–15 per cent. of all persons with gastric complaints. Its occurrence is independent of the acidity titre of the stomach; it is found more often associated with hyperacidity, but may occur in all grades of acidity, even in achylia gastrica. Most of the cases of hypersecretion are of the continuous type, lasting throughout digestion and the interdigestion period. The most severe type of cases, which are accompanied by vomiting, emaciation, thirst, epigastric pain, &c., constitute Reichmann's disease. Of the milder grades of hypersecretion about one-third are due to ulcer, and the rest are due to abnormal nerve irritation, either reflexly from abdominal disease or other organs, or from neurotic instability, such as vagotonia, psychoneurosis, &c. A few cases are due to diseases of the cerebral nervous system, hysteria, psychic causes, &c.

Berman, of New York, reports 11 cases of hyperchlorhydria in children aged from 2 to 6 years, in whom a series of gastric examinations were made by a modification of the Töpfer procedure, gastric juice being obtained one hour after a test meal consisting of a few biscuits and a glass of water. The symptoms consisted of (1) disturbance of appetite, (2) abdominal pain, (3) nausea and vomiting, and (4) constitutional symptoms. All Berman's cases occurred in a certain type of child, generally dark-complexioned, with a tendency to low blood-pressure, low blood-sugar, and a relatively abnormal fatigability. Berman suggests that this type is due to a constitutional hypoadrenalism, in which gastric irritation and bad hygiene produce hyperchlorhydria, hyperperistalsis, or disturbances of peristalsis of the stomach and accompanying symptoms. All the patients did well under a general hygiene regimen with removal of the gastric irritants from the diet Antacids and adrenal nucleoprotein also assisted in the restoration of the condition.

Frenkel-Tissot, of St. Moritz, describes an example of familial gastromyxorrhoea in two sisters aged 40 and 44 and the latter's daughter aged 23.

Vagotonia was well marked in all three cases, especially mucous colitis and bronchial asthma, as well as bradycardia (spontaneous and after ocular pressure), respiratory arrhythmia, myosis, and hyperidrosis.

In a series of 684 consecutive cases admitted to Duff House, Banff, with symptoms of alimentary disturbance, Conran found **gastroptosis** in 150, or 22 per cent., the term gastroptosis signifying dropping of the lower border of the stomach to a point 10 cm. or more below the summits of the iliac crests. Gastroptosis was present in 56, or 11 per cent., of 425 men, and in 94, or 36 per cent., of the women examined. It was almost as frequent in childless women as in mothers. Conran suggests that the strain of menstruation may account for the greater frequency of the syndrome in women. Among 266 persons under 40 it was found in 51, or 19 per cent., and in 99, or 24 per cent., of 418 persons over 40. The presence of severe gastroptosis in young children indicated that the hypotonic diathesis of which gastroptosis was a manifestation might be congenital. The principal symptoms on admission were first and chiefly constipation; secondly, pain or discomfort coming on at irregular times and situated in the upper abdomen or left iliac fossa. The pain, discomfort, and constipation were usually closely associated. Thirdly, flatulence, mostly intestinal and associated with constipation, but often gastric and possibly due to aerophagy. Fourthly, a group of symptoms suggestive of toxaemia, such as loss of energy, headache, depression, insomnia, anorexia, bad taste, joint pains, susceptibility to cold, and emaciation. X-ray examination showed that gastroptosis was only one among many indications of a general loss or lessening of tone in the gastro-intestinal musculature. Dropping of the transverse colon usually accompanied gastroptosis, but dropping of the flexures was comparatively seldom found. An adequate diet, sufficient exercise, and constant attention to the bowels in childhood and adolescence are the most important points in prophylaxis. Treatment consists in a lacto-vegetarian diet, paraffin, and abdominal massage with possibly electrical treatment, and, if the condition is very severe, intestinal lavage.

Tuberculosis of the stomach. Two important papers have recently been published on this rare condition by Baetzner, assistant in Bier's Clinic at Berlin, and by Spengler, of the Sophia Hospital in Vienna, each of whom reports an illustrative case. According to Baetzner, the statistics of the Kiel Pathological Institute show that only eight examples of the kind occurred among 2,000 cases of tuberculosis, and Eisenhardt, among 6,000 cases of tuberculosis which included 600 examples of intestinal involvement, found only one case of tuberculosis of the stomach. Clinical cases are rarer still, barely two dozen being on record (Albu). The condition is usually secondary to pulmonary and miliary tuberculosis. The rarity of gastric infection is due to the physiological action of the gastric juice and the motility of the stomach, as well as to the anatomical structure of the organ with its rarity of follicles. The lesion usually found is an ulcer, which is situated most frequently at the pylorus and is liable to all the complications of ordinary gastric ulcer, such as haemorrhage, perforation, and fistula. The symptoms are those of ordinary gastric ulcer, viz. dyspepsia and motor and chemical disturbances. Baetzner's patient was a woman aged 38 who complained of severe pain half an hour after food. Nothing could be felt on palpation. Gastric analysis showed an absence of free hydrochloric acid and the presence of free lactic acid. On operation a tuberculous ulcer of the greater curvature was found. A transverse resection was performed, and the

patient remained free from symptoms for three months, when a recurrence took place, and posterior gastro-enterostomy was performed. Recovery was delayed owing to the occurrence of acute pulmonary symptoms. The issue of the case is not recorded. Spengler excludes all the cases of simple gastritis and the multiple small erosions and ulcers found in the terminal stage of severe phthisis, as well as the rare cases of miliary tuberculosis of the stomach, and concerns himself only with the gastric tuberculosis which leads to pyloric stenosis. He describes two principal forms, an ulcerative and a hypertrophic. In both forms the pyloric part of the stomach is the site of predilection. In addition to these two principal forms is a rare inflammatory sclerotic variety which may also give rise to pyloric stenosis. Extra-gastric causes, such as the formation of bands following tuberculous peritonitis or the pressure caused by tuberculous glands, may also occasionally produce pyloric stenosis. In Spengler's case, which occurred in a man aged 45, the coexistence of open pulmonary tuberculosis with signs of pyloric stenosis suggested the diagnosis of a tuberculous gastric ulcer, which was confirmed by operation. Death from exhaustion took place two days after gastro-enterostomy.

According to Böge, of Magdeburg, who reports a fatal case, in a woman aged 30, of diffuse submucous phlegmon of the duodenal wall which had involved the pyloric part of the stomach, the possibility of a **duodenal phlegmon** should be considered in the differential diagnosis of diseases in the region of the stomach, duodenum, pancreas, liver, and bile-ducts. The symptoms are constant violent vomiting of large quantities of bile, severe pain in the upper abdomen, abdominal distension and tenderness, jaundice, fever, and leucocytosis.

Yeomans, of New York, made the following observations on 65 cases of chronic **ulcerative colitis** of unknown aetiology. 35 were between 16 and 30, 13 between 31 and 40, 8 from 41 to 50, 5 from 51 to 60, and 4 61 or older. The youngest patient was 16 and the oldest 66. In 37 cases no definite cause could be assigned. In 5 cases there was a history of amoebiasis, but no amoebae or cysts were found in the stools, and full courses of emetin were beneficial in only one case. The onset dated from dietary indiscretions in 6, severe constipation in 5, exposure in 3, injury, pyorrhoea, root abscesses, and pregnancy in 2 cases each, parturition in 1, and surgical operation in 3. Several examinations of the stools were negative for *B. dysenteriae* (Shiga, Flexner), amoebae, cysts, ova, parasites, tubercle bacilli, and flagellate bodies. The Wassermann reaction was positive in 3, negative in 55, and not examined in 7, so that syphilis was not an important aetiological factor. Secondary complications were polypus in 4 cases, rectal stricture in 1 case, and arthritis or joint pains in 4 cases. The onset was gradual in 47 and acute in 18, with diarrhoea or rise of temperature. The number of the stools ranged from 3 to 20 in the twenty-four hours, the motions occurring mainly in the morning and evening, rarely in the night. The discharge consisted of blood alone in 10 cases, blood and mucus in 19, blood and pus in 12, and blood, pus, and mucus in 15. Hence blood predominated or was present in the discharges of 86 per cent. of the patients. Intestinal colic and urgency before the action of the bowels were characteristic symptoms, as were also a feeling of abdominal unrest and occasional tenesmus when the rectum was extensively involved. The chronicity of the process was indicated by the period during which the disease had existed before the patient came under observation, viz. 1 year in 29 cases, from 1 to 5 years in 28, from 6 to 10

years in 6, and from 11 to 15 years in 2. The average period was 2 years and 2 months. The diagnosis was easily made by the history, laboratory examination of the stools, sigmoidoscopy, and roentgenograms of the colon. Treatment was symptomatic and empirical. In the vast majority of cases it was medical at first, and later operation was indicated.

Bassler, of New York, who in the course of eight years has seen 92 cases of ulcerative colitis which he regards as due to *B. coli*, recommends the following mode of treatment: (1) a diet rich in protein and with a laxative action, even if diarrhoea is present, (2) transduodenal lavage with a hypertonic solution of 9 gm. each of sodium sulphate and sodium chloride in 1,000 c.cm. of water at 105° F., (3) employment of various dyes to act on the bacteria of the alimentary canal, especially gentian violet in the strength of from 0·3 gm. to 0·75 gm., which is added to the hypertonic solution. In addition to gentian violet in irrigations he has recently employed it in pills each containing 0·016 gm. after meals. Acriflavine in pill form also had a good effect on *B. coli*.

Einhorn (2) (3) reports two cases of ulcerative colitis successfully treated by irrigation of the colon from above by means of a new jointed intestinal tube in place of that previously employed by him (vide *Medical Science*, 1920, **1**, 591).

Under the title of **haemorrhagic erosions of the rectum**, Westphal, of the Frankfort Medical Clinic, records eight cases, in adults of both sexes aged from 30 to 47, of a hitherto undescribed condition which is probably often mistaken for piles or ulcerative proctitis. The symptoms consist in frequent attacks of sudden intestinal haemorrhage in the midst of health without any previous intestinal history. On rectoscopic examination there is no sign of inflammation of the mucous membrane, but the cause of the haemorrhage is found in a number of minute ulcers in an otherwise normal mucous membrane, ranging in size from a pin's head to a lentil or bean. The ulcers show a rapid tendency to heal as a rule, but occasionally perforation takes place. Late relapses sometimes occur. The lesions appear to be less frequently due to embolism or thrombosis of the corresponding vessels than to neurotic vaso-motor factors which lead to a persistent occlusion of the vessels. Treatment consists in injections of gelatin.

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J. D. R.

NEUROSYPHILIS

Aetiology. The existence of a distinct *neurotropic strain of S. pallida* maintained by Marie and Levaditi on the evidence of experimental inoculation in rabbits, and by others on the grounds of instances of neurosyphilis in persons infected from the same source and cases of conjugal neurosyphilis, is doubted by Kaliski and Strauss, who have observed that, of patients infected from the same source, some developed neurosyphilis while others did not. Also, an instance of familial tabes recorded by Burrow does not support the neurotropic theory. In this instance, out of six members of a family born of healthy parents, four contracted syphilis from different sources and developed tabes, a fifth apparently developed early tabes with a doubtful history of syphilis, the sixth escaped syphilis and remained healthy. Burrow explains these cases by special sensitization of the tissues, due either to family peculiarity or to the effect of treatment.

In an article on *syphilis and trauma*, Klander discusses the influence of head injuries in the development of general paralysis in old syphilitics. He gives details of three cases in which symptoms of general paralysis appeared shortly after severe injuries, and one in which it followed sunstroke. He remarks that the interval between the trauma and the paretic symptoms necessary for the case to be regarded as of traumatic origin is not definitely known, but is of medico-legal importance. Mott gives a week as the minimum, and Solomon and Southard three months as the maximum interval. With regard to the employment of syphilitics in respect of the Workmen's Compensation Act, Klander remarks that the risk is small in most cases, but greater in the case of neurosyphilitics. He points out the importance of pupil changes as early signs of neurosyphilis, but mentions that these may be absent. Examination of the spinal fluid is also uncertain, for from 30 to 40 per cent. of cases with isolated pupil phenomena have negative spinal fluids. In such cases the pupil change is probably a scar of cured neurosyphilis. On the other hand, pupil changes may long precede the outbreak of other signs of neurosyphilis, and, if the spinal fluid is positive, such cases will be likely to develop general paralysis after a head injury.

Fraser and Duncan consider that the alleged *increased incidence and earlier onset of neurosyphilis* is real, and due to modern arsenical treatment. In support of this contention they mention that neurosyphilis, which was previously unknown among the natives of South Africa, has appeared among them since salvarsan treatment was introduced. They have also observed cases of tabes which occurred as early as 2 to 18 months after infection. In attributing this increase of neurosyphilis to the effects of arsenobenzene, they assume that intensive arsenical treatment destroys the

spirochaetes in the general system, but not those in the nervous system, and that the latter flourish owing to deficiency in the supply of antibodies due to destruction of spirochaetes in the general system; the central nervous system being capable of little antibody formation and depending on the general system for its supply. Kaliski and Strauss criticize this view and hold that there is no scientific proof of the production of antibodies in syphilis, or of syphilitic immunity.

Another factor adduced by Fraser and Duncan is direct damage to the nervous system caused by the drug itself. This view is also held by Matzenauer, who attributes neurorecidives after large doses of arsenobenzene to injury to the vessels by the action of arsenic.

Sézary discusses the *pathogeny of general paralysis and tabes.* He points out that the lesions of these affections differ from other syphilitic lesions histologically, therapeutically, microbiologically, and serologically. Histologically, the changes consist of perivascular and intestinal inflammation and changes in the nerve elements, with an absence of any tendency to sclero-gummatous formation. Therapeutically, they are resistant to treatment by arsenic and mercury. Microbiologically, the spirochaetes are found in the nerve element, not in the meninges. Serologically, the Wassermann reaction in the blood is reducible; in the spinal fluid it is irreducible. In attempting to explain these facts, Sézary remarks that the hypothesis of the neutropic virus will not explain the histological peculiarities, nor the resistance to treatment. Spirochaetes from the brain of a general paralytic inoculated in the rabbit are destroyed by treatment of the animal. The theories of anergy and hypersensibility he regards as very doubtful. He believes that the nervous tissue, being much less susceptible than the rest of the body to the action of antibodies, behaves as a non-immunized soil when attacked by the spirochaetes, and compares it to the chancre. The nervous system, he holds, by reason of its chemical constitution, escapes the action of immunizing bodies. Hence, general paralysis does not undergo spontaneous cure like the chancre. The Wassermann reaction in the blood is reducible because it obeys the general law, while the spinal fluid is irreducible because the antibodies are continually drained away by the perivascular lymphatic sheaths. Sézary concludes that the nervous tissue possesses a certain natural immunity against the spirochaete, but this is only sufficient to retard its development. On the other hand, the nervous tissue does not share the immunity acquired by the rest of the body. Thus, the spirochaetes which have invaded it are protected, become adapted to their environment, and eventually give rise to lesions which are atypical because they escape the humoral factor which controls the usual syphilitic process.

Diagnosis. Kaliski and Strauss are of opinion that there is a tendency to overestimate the importance of changes in the spinal fluid as indications of pathological changes in the central nervous system. From examination of thousands of fluids in syphilitic and non-syphilitic cases, with and without definite involvement of the central nervous system, they conclude that 8 to 10 lymphocytes per cubic mm. is within the normal, and that a slight increase above this with no clinical signs, no increase in globulin, and a negative Wassermann reaction is probably of no significance. On the other hand, cases of definite neurosyphilis often show no increase of cells. Increase of globulin, which is generally proportional to the increase in cells, they consider of little importance by itself. Of greater importance is

a positive Wassermann reaction, especially if present in all dilutions from 0·1 c.cm. upwards. In short, these observers believe that pleocytosis and increased globulin with a transient Wassermann reaction signify a temporary reaction due to limitation of the pia-arachnoid, of doubtful significance as regards future neurosyphilis. Pleocytosis, increased globulin, and a definite Wassermann reaction in all dilutions in early syphilis, however, they regard as probably the earliest signs of neurosyphilis.

With regard to the time and manner of infection of the central nervous system, Kaliski and Strauss remark that morphological evidence is lacking and biological reactions are inconclusive. The theory that spirochaetes enter the central nervous system in the early stages of infection, lie dormant, and subsequently multiply in response to some unknown stimulus they consider to be non-proven. It is possible that the spirochaetes wander into the central nervous system later, and, finding a less resistant or more fertile soil, multiply therein.

Fraser and Duncan also dwell upon the inconclusiveness of the biological reactions and consider that in the absence of clinical signs a normal spinal fluid may indicate either success or failure of the central nervous system to react, and that a pathological fluid may indicate either damage or protective reaction, and thus cannot be decided in the absence of symptoms. Clinical evidence must, therefore, be correlated with laboratory findings.

Solomon and Klander urge the importance of *clinical diagnosis* in neurosyphilis, as the spinal fluid may be negative in cases of active disease. According to these observers, the clinical types in which the fluid is often negative are: (1) vascular syphilis with thrombosis, haemorrhage, cerebral aneurism, or arteritis obliterans; (2) tabes, cerebral gumma, cranial paralysis, Erb's spastic paraplegia, syphilitic epilepsy, and syphilitic dementia. Of the chief points in diagnosis, the Argyll Robertson pupil is diagnostic of neurosyphilis, but sluggish reaction and irregularities in the form of the pupil are suggestive but not pathognomonic of syphilis; however, if they occur in a known syphilitic they are probably syphilitic in origin. The same with aphasia, reflex disorders, affection of the cranial nerves, convulsive attacks, &c. The Wassermann reaction in the blood may be either positive or negative in these cases. As regards the spinal fluid, the authors mention the statement of Head and Fearnsides that in pure cerebral syphilis, without implication of the cord, the fluid is nearly always negative. In a previous study of 28 autopsies, Solomon showed that the gold test varied in the fluid taken from different parts of the brain; further experience has shown that this applies to the other tests and the globulin content, the cell count, and the Wassermann reaction. In general paralysis, for example, the fluid from the ventricles may be negative and the lumbar fluid positive. In the absence of pathological changes in the spinal fluid, the best test, according to Solomon and Klander, is a provocative injection of arsphenamine, which will render the fluid positive if neurosyphilis is present. They regard a negative spinal fluid in progressive tabes as evidence of a primary degeneration of the posterior columns, with no inflammatory lesion. Other cases of tabes which may have negative spinal fluids may be abortive cases, usually confined to pupil changes, or cases arrested by treatment.

According to Keidel and Moore, the *cerebrospinal fluid* in early untreated syphilis shows pathological changes in 30 to 50 per cent. of cases, although a positive Wassermann reaction is only obtained in from 1 to 4 per

cent. They differentiate four groups of spinal fluids in syphilis: (1) Cases with normal fluid, the majority of which remain free from clinical or serological evidence of neurosyphilis. (2) Cases with pleocytosis, increased globulin, and a negative Wassermann reaction. In these there may be meningeal irritation without tissue invasion. Such cases do well on routine treatment without intraspinal treatment. (3) Cases showing further increase of globulin and pleocytosis up to 50 cells; negative Wassermann reaction with a small quantity of fluid, sometimes positive with a larger quantity; gold test of the 'syphilitic' or 'meningitic' type. These cases generally do well on ordinary treatment, but the authors advise that arsenical treatment should be continued for longer periods and administered at shorter intervals. They consider that the spinal fluid changes of this type probably indicate future meningo-vascular cerebrospinal syphilis. Headache is frequently present in this group. (4) In this group the number of cells is more than 50 and the globulin further increased. The Wassermann reaction is positive with 0·2 c.cm. of fluid and the gold test is of the 'paretic' type. Routine treatment is usually insufficient, and if no improvement occurs after six months intraspinal treatment is indicated. Even then progress is slow. This group probably represents future parenchymatous syphilis. Two cases in which this developed while under observation are mentioned. Keidel and Moore believe that a persistent positive Wassermann reaction in the blood is a probable indication of neurosyphilis.

Treatment. Kaliski and Strauss deprecate the modern tendency, supported by Fordyce and others, to treat the biochemical reactions of the disease instead of the clinical symptoms. In early cases of cerebrospinal syphilis, early tabes, and general paralysis they give intravenous injections of arsenobenzene, on an average, every 5 days till acute symptoms subside. They rarely give more than 0·4 gm. of arsphenamine or its equivalent. When the medulla, optic, or other cranial nerves are affected, arsenical treatment is preceded by one or two soluble mercurial injections (chloride or succinimide). In more chronic cases arsenobenzene is given once a week in doses of 0·25 to 0·4 gm.

Intraspinal treatment they consider of very limited value, for the following reasons: (1) The amount of arsenic present in auto-salvarsanized serum is infinitesimal and of no spirochaeticidal value. (2) There is no proof that salvarsanized serum is spirochaeticidal *in vivo*. (3) It is impossible to reinforce blood serum with more than an infinitesimal amount of salvarsan. (4) The direct introduction of any arsenical compound into the cerebrospinal fluid is dangerous, and if non-toxic is impotent. (5) The pathological changes in neurosyphilis are rarely only superficial, and are not reached by injection into the subarachnoid space. (6) The method is physiologically wrong. The cerebrospinal fluid serves as a hydrostatic agent for suspension of the brain and cord and as an avenue of excretion, not for nutrition of the cerebrospinal tissues. Hence, medication of the nervous tissues through the cerebrospinal fluid is impossible. Substances introduced into the cerebrospinal fluid are rapidly absorbed into the blood and rarely diffuse through the subarachnoid space. The direction of flow in the perineuronal lymph spaces is away from the nervous tissue and towards the cerebrospinal fluid. The pressure in the cerebral capillaries is greater than that of the cerebrospinal fluid. (7) Arsenic injected intravenously reaches the cerebrospinal fluid in greater quantity than can be injected intraspinally without damage to the nervous tissue. (8) In acute

or chronic meningitis 'antibodies' from the blood reach the subarachnoid space. Intraspinal injections may render the secreting mechanism more permeable, by irritation. Spinal drainage may act in the same way, as well as by reducing pressure.

They conclude that the presence of spinal fluid changes in early syphilis does not indicate the necessity for intraspinal treatment, because these changes are generally transient, do not in most cases signify neurosyphilis, and generally clear up under the usual form of treatment. Intraspinal treatment they reserve for the rare cases in which, after a few years of proper treatment, all the reactions in the spinal fluid are unchanged. As regards general paralysis they regard intraspinal and intracranial treatment as futile; but, as some cases may prove to be more hopeful cerebral syphilis, they recommend persistent treatment by intravenous injections of arsenobenzene and mercurial inunction or injection.

With regard to lumbar puncture, they consider that this should be done in all cases of early syphilis at the end of the first year of treatment, or earlier if there is clinical evidence of neurosyphilis. If negative it need not be repeated till the third or fourth year. If positive, it need not be repeated more than once a year. Too frequent punctures may do much harm. In this connexion a case reported by Klander is of interest, in which the site of repeated lumbar puncture developed into a syphilitic ulceration.

Schaller and Mehrtens have compared the results of intraspinal treatment (Swift, Ellis, Ogilvie, and Byrne's methods) with intravenous treatment and with the combined method of intravenous injection and spinal drainage advocated by Dercum (*Medical Science*, 1921, **4**, 338). While more in favour of intraspinal treatment than Raliski and Strauss, they agree that it is of limited application. They conclude that treatment should be commenced with intensive intravenous and intramuscular injections, especially in vascular and meningovascular neurosyphilis; that drainage combined with intravenous injections is indicated when there are distressing symptoms of increased spinal fluid pressure; that intraspinal treatment should be reserved for cases resistant to the above methods, especially tabes; that cases of neurosyphilis without reactions in the spinal fluid are not benefited by intraspinal treatment. They confirm the results of other observers in finding arsenic in the spinal fluid in 42 per cent. of cases treated intravenously.

Sézary believes that arsenobenzene only acts on the spirochaetes when it undergoes oxidation by the tissues, and that the brain has a reducing instead of an oxidizing action, which explains the incurability of general paralysis. The same explanation may apply to mercury. As regards intraspinal treatment, Sézary thinks it is of doubtful value, because it is not certain that the drug undergoes the necessary oxidation in the cerebrospinal fluid, nor that this is the best route to reach spirochaetes situated in the central parenchyma. He thinks it better to introduce the drugs by the way in which the spirochaetes entered, the general circulation.

Balina reports three cases of *tabetic optic atrophy* in which vision was improved by arsenico-mercurial treatment. The improvement was maintained during the period of observation, in one case for $2\frac{1}{2}$ years. The length of time between the onset of failing vision and treatment was 1, 2, and 6 years respectively. The treatment consisted in intravenous injections of cyanide of mercury and neosalvarsan administered in the following way: mercurial injections of 1 to 2 cgm. daily for 10 days, afterwards 2 or 3 times a week, to a total of 20 or 30 injections; arsenical injections com-

menced after the tenth day, in doses of 10 cgm. increased by 5 cgm. each time, given every 2 or 3 days between the mercurial injections, and continued alone after the mercurial injections in doses of 0·6 gm. every 5 days to a total of 10–12 gm. neosalvarsan. The author remarks that his results tend to show that in tabetic optic atrophy the destructive process is not complete and is partially amenable to repair, also that neosalvarsan does not damage the optic nerve, but may even cause improvement when it is affected with syphilis.

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C. F. M.

THE BIOCHEMISTRY OF THE BLOOD IN RELATION TO ITS CALCIUM AND PHOSPHATE CONTENT

The introduction during recent years of various methods by which the calcium and inorganic phosphate content of the serum or blood can be estimated in small amounts of material has led to the appearance of numerous papers dealing with the amounts of these bodies normally present and the variations which occur in disease.

Methods

Calcium. In estimating the calcium content of the serum, or blood, it has been customary to obtain a solution from which calcium may be precipitated, either after destruction of the organic matter present by ashing

or digestion, or by precipitation of the proteins by picric, tungstic, or trichloracetic acids. Recently, however, the method of direct precipitation originally devised by Pribram has been re-introduced, thereby greatly simplifying the estimation. In all methods the calcium is ultimately precipitated as an oxalate, and the washed oxalate is then estimated, (1) volumetrically, by titration with potassium permanganate; (2) nephelometrically, as a calcium soap; or (3) colorimetrically, by decolorization of ferric thiocyanate. The gravimetric method is of course only applicable to comparatively large quantities of material and the iodometric method of Jansen does not appear to have been extensively utilized.

The available methods have recently been reviewed by Clarke, who adds a new method of his own, in which direct precipitation is employed. He concludes from his experimental work that direct precipitation of the total calcium from serum is feasible, and that the permanganate titration, if certain conditions be observed, is accurate to approximately 2 per cent. The values obtained by the direct precipitation method agreed well with those obtained after ashing in platinum, the method which is usually accepted as the standard for comparison, though, even in this method, there is danger of loss by spluttering during incineration and by failure completely to dissolve the fused residue. The deproteinization methods gave in his hands unsatisfactory results. The time required for complete precipitation of calcium from serum as oxalate is over three hours. The number of washings of the precipitate must be limited, since calcium oxalate is appreciably soluble in water, and for this reason centrifugalization is preferable to filtration. He was unable to satisfy himself that calcium could be accurately determined, by nephelometry, as calcium stearate (Lyman's method). In this latter conclusion Halverson, Mohler, and Bergeim, and Meigs and his collaborators concur.

Kramer, Tisdall, and Howland, who have had a large experience in the determination of blood calcium, discuss briefly possible errors in current methods. They point out that if solutions of serum ash are rendered alkaline with ammonia there is a danger that calcium may be precipitated as a phosphate. The magnesium of the serum is too small in amount to be a serious source of error. In their own method they precipitate calcium directly from diluted serum, and obtain figures for normal individuals which, as will be seen later, fall within the usually accepted limits, though Clarke is inclined to believe that the time which they allow for precipitation is inadequate.

Mention may be made here of a biological method of estimating the calcium of blood devised by Vines. The principle of this method lies in the recalcification of oxalated blood by addition of varying amounts of the material to be tested and a comparison of the action of the latter in producing clotting with that of calcium chloride solutions of known strength.

Those interested in the question of the reliability of the various suggested methods of estimating calcium in serum should consult Clarke's paper, where the difficulties met with in this micro-estimation are fully discussed, and where they will find a good bibliography of the subject. It need only be remarked here that the pitfalls are numerous, and that anomalous results must be accepted with caution. The consensus of opinion appears to be in favour of a marked constancy in the serum content of calcium under normal conditions, and methods which give a wide range of serum calcium in the healthy individual should therefore be regarded with

suspicion. This objection appears to apply particularly to the nephelometric method of Lyman, which has enjoyed a considerable vogue in America, but which has been unfavourably reported upon by several workers who have studied it from a critical standpoint. There appears to be satisfactory evidence in favour of the accuracy of methods in which direct precipitation and permanganate titration are employed, and such methods have the additional advantage of rapidity and simplicity.

Phosphates. In the estimation of inorganic phosphates in small amounts of blood the nephelometric method of Bloor has been, until recently, that most generally employed. Two colorimetric methods have now been introduced, which, in view of the greater simplicity and possibly greater accuracy of colorimetry as compared with nephelometry, may ultimately replace Bloor's method. In the technique devised by Marriott and Howland, the phosphates are colorimetrically determined by decolorization of ferric thiocyanate, while, in the simple and rapid method of Bell and Doisy, the colour reaction that occurs between phosphomolybdic acid and hydroquinone is utilized. Modifications have been suggested in the Bell-Doisy method by Lehmann ; and Myers and Shevky find the original method unsatisfactory, and suggest certain alterations with a view to greater accuracy. Denis, who found it satisfactory for the determination of urinary phosphates, states in a recent paper, written in collaboration with von Meysenburg, that she is convinced of the reliability of the method in the estimation of the inorganic phosphates of serum, but that in determinations of plasma the added citrate or oxalate must be strictly limited, and the molybdic reagent added in larger amount. Unless these precautions are taken the values found will be too low.

The Calcium Content of the Blood and its Distribution.

Most modern work appears to show a fair agreement as to the average concentration of calcium in serum or plasma. Kramer, Tisdall, and Howland find 9·3 to 11·0 mgm. per 100 c.cm. of serum in man ; Halverson, Mohler, and Bergeim, 9·6 to 10·8 ; Vines, in eight adults, 10·2 to 10·7 ; and Howland and Kramer, 9·3 to 9·9. For children, Kramer, Tisdall, and Howland give slightly higher figures, 10–11 mgm., while Jones and Nye find an average value of 10 mgm. The work of these latter authors, who used Lyman's nephelometric method, shows a far wider range of calcium values in the normal child than does that of other investigators. Thus, in 17 normal boys, the calcium content of the plasma ranged from 5·5 to 14·4 mgm. per 100 c.cm. Jones, in a series of observations on the plasma calcium of infants from four hours to twelve days after birth, found an average value for plasma of 12·3 mgm. The calcium average remained constant during the first twelve days of life. A few additional figures showing the comparatively constant calcium content of mammalian serum may be given here. In cows, Meigs, Blatherwick, and Carey found 9 to 11 mgm. per 100 c.cm. ; in dogs, Hastings and Murray give a value of 10 to 12 mgm. ; and in rabbits Watanabe found 10 to 13 mgm. Recent work appears to suggest that in the mammalia the serum or plasma calcium is maintained at a remarkably constant figure (about 10 mgm. per 100 c.cm.), and that deviations from this figure, whether in health or disease, need very convincing demonstration if they are to be regarded as proved.

It has been generally accepted that little or no calcium is present in the corpuscles. Howland and Marriott, who found about half as much

calcium in the whole blood as in serum, concluded that there was no calcium in the corpuscles, a conclusion which was in agreement with the earlier analyses of Abderhalden. Cowie and Calhoun, on the other hand, using Lyman's method, found as much as 4·26 mgm. per 100 c.cm. corpuscles, and Jones and Nye by the same method have found even higher figures, the corpuscular calcium exceeding, in some instances, that of the plasma. These findings appear to need further confirmation, and, in any case, determinations of serum or plasma calcium would appear to be of greater value than estimations on the whole blood. In dealing, therefore, with a substance which is certainly unevenly distributed between plasma and corpuscles, and may be absent from the latter, we have, if we are to draw any deductions from estimations on the whole blood, to add to our findings haematocrit readings which in themselves introduce an additional error.

That part of the serum calcium is present in a non-diffusible form was first conclusively demonstrated by Rona and Takahashi. Von Meysenburg and his collaborators have recently re-investigated this question, dialysing serum, under constant CO_2 tension, against a buffer solution of the Ringer type. If calcium is added to the dialysing solution, equilibrium is established between the two fluids in 24 hours, and the diffusible calcium amounts to 60 or 70 per cent. of the total serum calcium. Dialysed against a calcium-free Ringer solution, a progressive dissociation of the colloidal calcium compound appeared to take place, until at the end of seven days 90 per cent. has passed into the dialysate. The figure given for non-diffusible calcium agrees with the results of Cushny, who found that 30 to 40 per cent. of the calcium was not filtrable through collodion membranes under a pressure of 150 mm. Hg, though sodium and potassium filtered as solutions. Richter-Quittner, in an analysis of the ultra-filtration of blood constituents, also finds that one-third of the calcium is present in a non-filtrable form. The possible existence of compounds of calcium and protein is made fairly certain by recent work of Loeb, who finds that proteins at a reaction above their iso-electric point form compounds with monovalent and divalent ions. The calcium, which is presumably combined with protein, is, however, loosely bound, since it can apparently be precipitated quantitatively from serum by the addition of ammonium oxalate.

Effect of administering Calcium Salts on the Calcium Content of the Blood.

This question has been recently investigated by several workers. Denis and Minot find that, in man and in cats and rabbits, the calcium content of the serum is not usually increased by administering calcium salts *per os*; if, however, the initial calcium concentration is low, it may be raised by oral administration of calcium. Clarke, using the method of Halverson and Bergeim, could produce no appreciable effect on the blood calcium by feeding a calcium-rich diet to which calcium lactate had been added. Hypodermic injections of calcium hydroxide or chloride led to a definite increase in the calcium of the blood, an increase which was, however, purely transitory, the excess calcium being rapidly eliminated. Mason, administering 5 gm. doses of calcium chloride or lactate *per os*, found no increase in the calcium of the serum, as determined by Lyman's method, in the three hours following the dose. Meigs, Blatherwick, and Carey failed to increase the serum calcium of the plasma in cows by feeding calcium salts. No worker has apparently met with abnormally high calcium values

as the result of feeding calcium salts. As will be seen later, in discussing the calcium content of the serum in tetany and nephritis, there is fair evidence that, if the serum calcium is definitely reduced, calcium salts given by mouth are capable of restoring it to a normal figure, but it would appear to be impossible to raise it to an abnormally high figure. The explanation of this fact probably lies along the lines suggested by Marriott and Kramer, who give reasons for believing that calcium salts are present in the blood in practically saturated solutions.

The Inorganic Phosphate Content of the Blood.

The inorganic phosphate content of the plasma differs from the calcium in being definitely affected by the diet. This was brought out in Greenwald's early work, when a marked increase in the phosphate content was found after a meal. The effect of increased rations in raising the inorganic phosphorus of the plasma was also noted by Meigs, Blatherwick, and Carey in their work on cows. It is advisable, therefore, to obtain blood for phosphate estimations from patients who are in the fasting condition.

The most elaborate studies of the blood phosphorus have been made by Bloor and his collaborators, using the nephelometric method. They have found that in male adults the phosphorus present in the plasma as inorganic phosphate varies from 1·9 to 3·8 mgm. (average 2·8), and in females from 2·5 to 4·1 mgm. (average 3·1). The corpuscular content of inorganic phosphate is considerably higher, averaging 5·9 and 4·9 respectively, with a maximum figure of 8·6 mgm. In normal infants, during the first two weeks of life, the values were approximately the same. Jones and Nye, utilizing the same method, give closely similar figures for children. Denis and Minot give 1·2 to 3·1 mgm. for hospital patients. Hess and Gutman, working with the Bell-Doisy method in infants, found a range of 4·1 to 4·8 mgm. apparently in the whole blood. Howland and Kramer report an average inorganic phosphorus content of 5·4 mgm. in the serum of healthy infants, while in adults they found a lower figure (2·1 mgm.).

There seems, therefore, to be a fairly close agreement among different workers, using different methods, as to the normal inorganic phosphate content of human blood. Further work would appear to be necessary to determine whether a difference actually exists between the adult and the infant. As in the case of calcium, determinations on whole bloods are undesirable, owing to the wide difference in phosphate content between plasma and corpuscles. All authors are agreed that laked plasma is, for this reason, useless, and plasma, separated as quickly as possible after bleeding, is preferable to serum, since Howland and Kramer have shown that a rapid increase may occur in the inorganic phosphate content of serum standing on the clot. The plasma phosphate is, according to Rona and Takahashi, wholly dialysable.

Conditions under which Changes in the Calcium and Phosphate Content of the Blood occur.

1. *Tetany.* That a fall in the calcium content of the serum occurs in experimental parathyroid tetany was first demonstrated by MacCallum and Voegtlin, and was naturally correlated with the effect of calcium deficiency in heightening nerve excitability, as observed by Loeb. A similar fall in the serum calcium in infantile tetany was found by Marriott and Howland,

and has since been the subject of numerous investigations. It appears to be generally accepted that the calcium content of the serum is diminished in all forms of tetany—in parathyroid tetany, in infantile tetany, in the tetany which sometimes follows the therapeutic administration of bicarbonate (Howland and Marriott), in guanidine tetany (Watanabe), and in the tetany produced by phosphate injections. In addition, symptoms of tetany begin to appear in all these conditions when the serum calcium has been reduced to about the same level, namely, between 6 and 7 mgm. per 100 c.cm.

There is, however, evidence which suggests that this fall in the serum calcium is not the only factor involved in the production of tetany. Thus the occurrence of extremely low calcium concentrations has been noted in the serum of nephritis without the appearance of tetany: if these observations are confirmed, they will go far to prove that the diminution in the serum calcium is not in itself the primary factor in the production of the disease. Again, Binger was able to produce tetany in dogs by injecting mixtures of di- and mono-sodium phosphate with a P_H of 7·4, while solutions with a P_H of 1·6 failed to produce tetany, even though the serum calcium was reduced to a level at which symptoms of the condition might be expected to appear.

Loeb, experimenting on the effect of various ions on nerve excitability, found that Ca and Na were mutually antagonistic: to preserve a normal condition of irritability the ratio $\frac{Na+K}{Ca+Mg}$ must be maintained at a fairly constant figure.

The kations were not alone concerned, since various salts of sodium differed in their power of stimulating nerves. Monovalent anions appear to act in the same fashion as divalent kations, that is they depress irritability, while divalent anions and monovalent kations increase irritability. Hastings and Murray suggest, therefore, that in Binger's experiments the phosphate is not necessarily the only factor involved, but that the amount of sodium injected has also to be considered. Loeb's work would also explain the production of tetany by injections of sodium salts, and the finding of Munzer that convulsions are more readily evoked by injection of sodium phosphate and bicarbonate than by sodium chloride, an observation which has not been confirmed by Greenwald. The absence of tetany in nephritics with very reduced serum calcium would also be explicable along similar lines. The ion ratio is not upset in the required direction, the bicarbonate reserve of the plasma showing a great reduction, while in parathyroid tetany in dogs there is, according to Hastings and Murray, no reduction in the alkaline reserve of the plasma except immediately after the operation, and in the hyperpnoea which precedes the onset of convulsions. These latter authors have obtained no evidence in favour of the alkalosis theory of tetany either by direct P_H estimations of the plasma of parathyroidectomized dogs or from estimations of the alkaline reserve.

Freudenberg and Gyorgy have studied tetany from a different standpoint, that of the conditions in which calcium combines with the amphoteric colloids. As colloids, they employed strips of cartilage, fresh brain emulsions, and gelatine. The combination of calcium and colloid occurs more readily with a falling hydrogen-ion concentration or with an increase in the calcium ions present: it is inhibited by phosphate, and bicarbonate, and also by certain protein derivatives, among which guanidine, trimethyl guanidine, and certain amino-acids may be mentioned. They believe that calcium is

almost entirely in the colloidal combination form in the tissues, while in the blood both ionic and colloidal forms are present. Tetany they attribute to any disturbance in the relationship between these calcium fractions which leads to a reduction in the colloidal calcium of the nervous tissues.

The phosphate content of the blood in tetany was first studied by Greenwald in parathyroidectomized dogs. He found diminished elimination of phosphorus and a marked rise in the inorganic phosphorus of the blood. Watanabe has investigated in rabbits the calcium and phosphate content of the blood after guanidine injections. He employed Marriott's method, and found that a rise in the phosphate concentration usually followed an injection. This rise was accompanied in most instances by a fall in the calcium, which he believes to be a secondary phenomenon. Howland and Marriott, who examined the serum of a few children suffering from tetany, found no definite increase in the organic phosphate. Howland and Kramer, in children showing latent tetany (anodal reversal) and rickets, with a serum calcium of 7·5 to 7·8, found the phosphate low, and Kramer, Tisdall, and Howland have reached the conclusion that an increase in the inorganic phosphate of serum does not appear to be responsible for tetany, though, in cases of rickets complicated by tetany, there is a relatively high inorganic phosphate content as compared with cases suffering from uncomplicated rickets. The close clinical association of rickets and spasmophilia, and the fact that in rickets there is good evidence for a marked diminution in the serum phosphate, seems to be against the assumption that the reduction of serum calcium which characterizes tetany is secondary to an increase in the inorganic phosphate content of the serum. The statement of Jeppson and Klucker that the feeding of phosphates to normal infants and those with latent spasmophilia produces symptoms similar to active spasmophilia is not confirmed by Calvin and Borovsky. In doses of 0·55 to 0·60 gm. per kilo of body-weight per 24 hours, disodium and dipotassium phosphate neither activated latent spasmophilia nor produced symptoms of it. Even in patients who had just recovered from spasmophilia the condition did not recur on administration of phosphates.

Stheeman, using the method of de Waard, which is probably not very accurate, has studied the connexion of the facial sign of Chvostek and the altered reactions characterizing spasmophilia with the calcium content of the blood. He finds a low blood calcium in children showing the anodal reaction and the facial phenomenon. He finds also that the calcium may be diminished in a variety of conditions—enuresis, orthostatic albuminuria, nutritional disorders, acute disorders of stomach and bowel, &c. Handovsky, on the other hand, finds that in adults there is no difference in the calcium content of the serum of normals and of those patients who show Chvostek's sign. Von Meysenburg also believes that there is no connexion between anodal hyperexcitability and a low blood calcium: calcium feeding in large amount was apparently without effect on the anodal reaction. The calcium distribution in the plasma of parathyroidectomized dogs, with a diminished calcium content, does not, according to von Meysenburg and McCann, differ from the normal. About 60 to 70 per cent. of the diminished calcium is present in a dialysable form: the remainder is non-dialysable.

The effect of calcium salts, administered by the mouth, in raising the serum calcium content in cases of tetany has been demonstrated by Marriott and Howland. Using calcium chloride, they were able to show a definite and rapid rise in serum calcium with improvement in the symptoms of the

disease. In some cases an intermission of the salt led to a fall in the serum calcium with a recurrence of symptoms. Brown, MacLachlan, and Simpson, working with Lyman's method on the whole blood of infants suffering from tetany, studied the effect of intravenous injections of calcium lactate. An injection leads to a rapid rise in the blood calcium, associated with an absence of the mechanical and electrical signs of tetany for 7 to 10 hours, after which they rapidly return to their previous condition. A reaction varying from slight drowsiness to collapse follows the injection. They find a distinct correlation between the blood calcium and the electrical excitability. The therapeutic effect of occasional doses of calcium intravenously appeared to be less marked than that of cod-liver oil and phosphorus, but the total calcium administered would appear to have been much less than the amounts which were given by Howland and Marriott. The effect of calcium chloride by the mouth in increasing the plasma calcium has recently been confirmed in two cases of tetany by Denis and Talbot.

2. *Rickets.* The calcium and phosphate content of the blood in rickets has been investigated by Howland and Kramer. They found a calcium value for the serum, excluding frank cases of tetany, which either fell within normal limits or was only slightly reduced. In considering the cases in which a slight reduction was found, about 50 per cent., they point out that the possibility of a latent tetany has always to be considered. The phosphate, on the other hand, showed a marked reduction, averaging 1·9 mgm. per 100 c.cm., as contrasted with a normal figure for children of the same age of 5 mgm. Under treatment with cod-liver oil the phosphate was restored to an average figure of 5·5 mgm., and radiographs showed evidence of healing. The calcium content of the serum was unaffected. Relapses were accompanied by a fall in the phosphate value. They point out that 85 to 90 per cent. of bone ash is in the form of calcium phosphate, while from 10 to 15 per cent. is composed of calcium carbonate. They believe that calcium salts exist in the blood in nearly saturated solution, and that, with a fixed CO_2 content, precipitation of tertiary calcium phosphate would be rendered more difficult by diminution in the HPO_4 ion. Iverson and Lenstrup had apparently arrived independently at the conclusion that the plasma of rachitic infants was poor in inorganic phosphates: a conclusion which agrees well with recently published observations of McCollum, Shipley, and Park upon the effect of a deficient phosphorus content of the diet in the production of experimental rickets in rats. In experimental work upon rats, Kramer and Howland have found that if a diet deficient in phosphorus and in the organic factor contained in fats is administered the concentration of inorganic phosphorus in the serum is much diminished. The calcium is unchanged if an adequate amount is present in the diet, and rickets is regularly produced.

An interesting observation has recently been recorded by Hess and Gutman. Hess and Unger had previously shown that rickets in infants can be cured by frequent exposures to the sun's rays, and that in rats on rickets-producing diet the appearance of rickets could be prevented if they were subjected for short periods to sunlight. Studying the inorganic blood phosphorus of infants by the Bell-Doisy method, they found a normal level of 4 mgm. per 100 c.cm. They confirm the finding of Howland and Kramer as to the low phosphorus content of the blood of rachitic children, and find that on exposing such children to sunlight, without altering the diet, the blood phosphate rapidly (2 days) returned to normal. The interest of these

observations is obvious, since they furnish the first definite evidence of metabolic change in the human body brought about by the solar rays, and since they show that the curative change brought about by sunlight and by cod-liver oil is fundamentally the same.

According to von Meysenberg and McCann there is no change in the calcium distribution in the plasma of cases of rickets. Diffusible and non-diffusible calcium are present in normal proportions.

3. *Nephritis.* The first studies on the phosphate content of the blood in nephritis date from 1915, when Greenwald demonstrated an increase in the acid soluble phosphorus of the serum. This increase usually, but not always, accompanied a marked nitrogenous retention, but this retention did not necessarily also involve the phosphates. Howland and Marriott, who give a range of 1 to 3·5 mgm. as the normal, found a tendency to an increased inorganic phosphate content in nephritis. Death from nephritis occurred, however, in patients who showed no rise in the serum phosphate. In patients who showed an acidosis, as evidenced by a diminished plasma bicarbonate, a rise in the phosphate was invariably present, the maximum figure noted being 23 mgm. Accompanying the phosphate rise, a fall in the calcium (estimated by the ferric thiocyanate method) often occurred; it was not, however, proportional to the phosphate increase. According to their findings, the calcium in the serum may fall to as low a figure as 1 mgm. per 100 c.cm. of serum. Halverson, Mohler, and Bergeim, working on serum with their own method, have also found low values for calcium in cases of nephritis. They conclude that the serum calcium is almost always diminished in uraemia, but give no figures approaching those of Marriott and Howland, the lowest value observed by them being 6·8 mgm. The administration of calcium lactate by the mouth was followed by perceptible increases in the serum calcium, with improvement in the clinical condition, but similar increases were observed in cases to which no calcium salts were given. No abnormally high figures for calcium were ever noted after administration of calcium salts. They comment on the singular constancy of this element in contrast with other blood constituents. Howland and Marriott also advocate the use of calcium salts in this condition, on the ground that they are known to produce elimination of phosphates by the bowel and would therefore tend to keep down the phosphate content of the blood.

Denis and Minot have also studied phosphate retention from the standpoint of blood analyses. Using Bloor's method, they found values ranging from 1·2 to 3·1 mgm. per 100 c.cm. in the plasma of patients suffering from pathological conditions other than nephritis or cardio-renal disease. Of 68 cases of cardio-renal disease, two-thirds gave unmistakable evidence of phosphate retention, the maximum figure noted being 43·7 mgm. They find that in patients who show a high non-protein nitrogen content in the blood, and an extremely low phenol-sulphonephthalein excretion, but no great increase in the phosphates, the prognosis is relatively good. Many fatal cases show a rapidly rising plasma phosphate. They could find no definite relation between the alkali reserve and the plasma phosphate, and state that sodium bicarbonate medication has no effect on the phosphate content.

A recent paper by Mayrs also suggests that a study of the plasma phosphate may be of some value in the prognosis of renal disease. Working on the relative concentration from blood to urine of urea, sulphates, creatinin, and phosphates, he found that the relative concentrating power of the kidney for the three latter substances was greater than for urea.

A more advanced degree of renal failure would therefore be necessary before these bodies could accumulate in the blood, and it is probable that a phosphate retention would have the same significance as a creatinin retention, a condition which is accepted by most workers on the subject as being of serious prognostic import.

4. *Miscellaneous conditions.* Denis and Talbot, taking 19 children at random from hospital wards, and determining the calcium content of the citrated plasma by Lyman's method, find a range of variation from 1 to 13·5 mgm. Some of their lowest figures were obtained in such unconnected conditions as petit mal, lobar pneumonia, infectious diarrhoea, chorea, influenza, and miliary tuberculosis. Their tables lead to the conclusion that practically any morbid condition in the child may be accompanied by a greatly diminished plasma calcium, but that this diminution need not necessarily occur in any of the conditions studied, with the exception of tetany. They were unfortunately unable to make any observations on strictly normal children.

Kramer, Tisdall, and Howland express disagreement with these findings, and contend that in children the serum calcium is singularly constant, except in cases suffering from tetany and nephritis. They suggest that the extreme susceptibility of tissues to changes in the inorganic content of the tissue fluids is against the acceptance of such results. Halverson, Mohler, and Bergeim, who studied the serum calcium in a variety of lesions in adults, believe that values below 8 mgm. are rare, and only found significant diminution in nephritis, eclampsia, and tetany. In view of the doubts expressed above as to the reliability of Lyman's method, it would appear to be wise to accept such results as those of Denis and Talbot with considerable caution. The statement of Hess and Killian, that the serum calcium is diminished in infantile scurvy, is also not confirmed by Kramer and his co-workers, and Halverson, Mohler, and Bergeim found a normal range in cases in which the clotting power of the blood was markedly disturbed. Krehbiel, utilizing the method of Halverson and Bergeim, and investigating the calcium content of the serum in a number of diseases, found low values in tetany, nephritis, and eclampsia. The lowest figure found, 4·29 mgm. per 100 c.cm. of serum, occurred in a case of eclampsia. In carcinoma the calcium value was normal. It may be noted that in diabetes, according to the findings of this author and of Halverson, Mohler, and Bergeim, the calcium of the blood is not depleted.

Meigs, Blatherwick, and Carey have examined the effect of pregnancy and lactation on the calcium and phosphate content of the blood in cows. They found that the calcium of the serum remained practically constant during pregnancy and lactation. In newly-born animals the calcium of the plasma was at an unusually high level. The inorganic phosphorus of the serum tended to fall during pregnancy, but rose during lactation, and apparently showed some relationship to the milk yield. From comparative analysis of the blood of the mammary and jugular veins, they conclude that the phosphatides of the blood are the source of the milk fat, and that in the active mammary gland the phosphorus is split off from the phosphatide and returned to the blood-stream in an inorganic form. They believe that a similar process goes on in muscle during activity, but Embden has produced evidence that the production of phosphoric acid in muscle is accompanied by the liberation of an equimolecular amount of lactic acid, both acids being derived from hexose phosphate.

Kehrer, using an ashing method, finds a definite fall in the calcium of the whole blood during the latter half of pregnancy: in cases of nephritis, complicating pregnancy, and of eclampsia he found extremely low calcium values.

The blood calcium has been studied in various ulcerative conditions by Vines: among these, varicose ulcers, gastric and duodenal ulcers, and erosions of the cervix were examined. He finds that in these conditions the ionic calcium of the blood and sometimes the total calcium is diminished. In the treatment of varicose ulcers administration of calcium salts proved ineffective, but parathyroid therapy led to rapid improvement with a return of the serum calcium to normal.

To sum up, the evidence suggests that the calcium content of serum is singularly constant. This constancy is probably due in the first place to the fact that at body temperature and at the CO_2 tension of the blood the serum calcium is present in approximately saturated solution: hence the impossibility of raising the calcium concentration of the serum by administering calcium salts. On the other hand, the reserve of calcium in the tissues of the body, especially the bones, is so great that reduction of the serum calcium is difficult, and, when it occurs, is conditioned rather by changes in the constitution of the fluid in which the salt is dissolved than by actual depletion of the body reserves. Such a change is seen when the phosphate or bicarbonate content of the serum is increased, and is possibly the result of the conversion of more soluble salts of calcium into the relatively insoluble calcium carbonate, or tertiary calcium phosphate. A diminution in the phosphate may, on the other hand, in rickets, lead to a lessened formation and precipitation of tricalcic phosphate. An additional complication is also introduced by the presence of colloidal combinations of calcium with the proteins of the blood. That the calcium of the serum is markedly reduced in tetany, and to some extent at least in nephritis, appears to be proved: evidence of a low calcium content in other pathological conditions is unsatisfactory.

The inorganic phosphate content of the plasma is, on the other hand, relatively inconstant and is to some extent affected by the diet. An increase in this blood constituent is seen in nephritis, probably as the result of diminished elimination, while a decrease is found in rickets. In this latter disease we have lately obtained the first chemical evidence of a change in the metabolic processes of the human being as the direct result of heliotherapy.

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O. L. V. de W.

ABSTRACTS

SURGERY

Sauer, P. K. Treatment of surgical tuberculosis with the carbon-arc lamp. *Ann. Surg.*, 1922, **75**, 400–3.

Sauer, impressed by the work of Reyn and Ernst in Copenhagen, has been using the carbon-arc lamp for the treatment of surgical tuberculosis with marked success. He finds it as effective as natural sunlight, with the advantage of independence of the weather and locality. He believes it to be just as effective as X-rays without their attendant dangers; he agrees with Reyn that it is more effective than the quartz-mercury vapour lamp. The lamp that he uses is a twin-arc lamp with a reflector, the arcs being connected in series. A current of 25 ampères and 110 volts passes through these carbons, thus giving each carbon half the voltage. The rays pass straight to the patient without the intervention of any glass. Each carbon is of a special chemical-core type. The affected part and its surroundings are exposed to the light as close to the lamp as can conveniently be borne by the patient, having regard to the heat. As the skin becomes more pigmented it is found that the patient can tolerate the lamp at a shorter distance. The time of exposure varies with the age, sex, and pigmentation of the patient; as a rule, a dark, male, adult patient can begin with $\frac{1}{2}$-hour exposure; children should not have more than $\frac{1}{4}$-hour at first. Three treatments a week should be administered, gradually increasing in length up to $1\frac{1}{2}$ hour as the patient becomes more tolerant. Pigmentation, without blistering, is to be aimed at. The rays from the quartz-lamp belong almost entirely to the ultra-violet end of the spectrum, not very penetrating but very irritating.

He gives notes of seven cases so treated, the number of treatments varying between 70 and 160. The number of cases treated upon which an opinion might be formed seems small, and a method of treatment that involves over 100 attendances on the part of the patient must be wearisome. The diseases included tuberculous osteitis, glands in the neck, tuberculous peritonitis, and tuberculous kidney. One case of glands in the neck is noted as 'not improved', the others are noted as 'cured' or 'improved', the latter two cases (viz. tuberculous kidney and tuberculous cervical adenitis) ceased attending, the one after twenty-five and the other after twenty-four visits.

C. C. C.

Hansen, S. Undersögelser over Cholelithiasis. [**Studies in cholelithiasis.**] *Ugesk. f. Læger.*, 1922, **84**, 405–21.

Hansen has systematically examined the biliary system in every case coming to necropsy in his hospital in 1920 and the first nine months of 1921. Only persons over the age of 20 were included in this material; this consisted of 1,191 bodies, among which gall-stones were found in 293, i. e. in 25 per cent. Hansen notes that his predecessor, Scheel, at the same hospital, found gall-stones only in 15 per cent. of a somewhat greater number

of consecutive necropsies. The literature of the subject shows the frequency of gall-stones found *post mortem* to range from 1 to 18 per cent.; this amazing difference probably does not depend on racial, dietetic, and other aetiological factors, but simply on the care with which gall-stones are sought and their discovery is recorded. After eliminating all the cases in which the gall-stones were the cause of death, Hansen still finds the incidence of gall-stones as high as 21·2 per cent. The differences in the sex incidence were remarkably small, considering that, among the cases coming to operation, the ratio of males to females has been estimated at from 1 to 4 and 1 to 9. In Hansen's material, gall-stones were found in 19 per cent. of the men and 31 per cent. of the women, i. e. a ratio of only 2 to 3. The reason for this disagreement between the pathologist and the surgeon is probably to be sought in the comparative frequency with which gall-stones in women give rise to serious symptoms in connexion with pregnancy and its after-effects. With regard to the age incidence, the frequency of gall-stones increased steadily in both sexes up to the age of 50; above this age there was little further rise in women, whereas in men the subsequent rise was so steep that the incidence was more than doubled in 20 years. As early as the age period 30–40 the incidence of gall-stones in women was as high as 20 per cent.

To show the comparative frequency with which the different kinds of gall-stones are found (*a*) *post mortem* and (*b*) at operation, Hansen publishes the following table, the figures under 'operation' being taken from Rovsing's work in 1900:

	Post mortem.	Operation.
Solitary stone	34	55
Multiple mixed stones	163	233
Pure pigment stones	58	18

In both series the multiple mixed stones were in the majority, particularly at operation, whereas the pure pigment stones were comparatively frequent as post-mortem findings. These stones must, therefore, be regarded as the most harmless, the multiple mixed stones as the most harmful. The comparative importance of these two classes is also shown by the biliary passages being healthy in the overwhelming majority of cases with pure pigment stones, whereas in over 50 per cent. of the cases with multiple mixed stones morbid changes were found in these passages. This finding supports the hypothesis advanced in 1893 by Lange, that pigment stones have an aseptic origin. However, in 14 of the 58 cases of pure pigment stones inflammatory changes were found in the gall-bladder. A table indicating the positions in which the gall-stones were found shows that in 215 out of the 293 cases the stones were confined to the gall-bladder. In 9 cases the stones had been removed by operation before the necropsy or were found in the intestine. There remained 69 cases, i. e. over 23 per cent. of the total, in which stones were found in the biliary passages. Hansen stresses this last finding as a serious warning to surgeons who do not systematically examine all the biliary passages, notably the choledochus, for stones.

In 167 cases, i. e. in 57 per cent., changes were found in the biliary passages which could be traced to the stones. In 10 cases small stones were also found in the walls of the gall-bladder as well as in its cavity, but only in 2 cases were foreign bodies found with the stones. In 24 of the 51 cases in which stones were found in the choledochus, there was no retraction of the gall-bladder. Retracted, occluded gall-bladders, containing no bile, and

obviously completely out of action, were often found, and in 48 of these cases, i. e. in about 70 per cent., there was a definite dilatation of the choledochus. In 15 of these 48 cases the dilated choledochus contained stones, but in 13 of these 15 the stones were loose, and were probably rather a sequel to, than a cause of, the dilatation of the choledochus.

In 18 cases stones were also found in the urinary system. But as stones in the urinary system, but not in the biliary system, were found in 34 cases, no relationship could be established between the two systems in this respect. In 126, or 43 per cent., the biliary system was healthy apart from the stones. In no fewer than 40 cases the cholelithiasis caused the patient's death; in the same period only 26 patients, whose death was due to appendicitis, were examined *post mortem*. Nine of the 40 deaths from gall-stones occurred on the *medical* side of the hospital.

Hansen considers that these findings justify a serious reconsideration of the whole subject of cholelithiasis. At present, cases of cholelithiasis are frequently 'nursed' by the physician till the patient's death from one of the direct sequels to cholelithiasis, or they are handed over to the surgeon too late. Cholelithiasis, in fact, 'enjoys' at the present time the status of appendicitis some decades back, and the ratio of cholelithiasis to appendicitis deaths (40 to 26) is an index to the comparative backwardness of the treatment of the former. The physician who depends on typical biliary colic and jaundice for his diagnosis of cholelithiasis must often overlook this condition, mistaking the symptoms for those of gastric or duodenal ulcer and the like. He would do well to examine the urine for urobilin, and to bear in mind that 25 per cent. of all adults harbour gall-stones. C. L.

McNee, J. W. Syphilis of the stomach. *Quart. J. Med.*, 1922, **15**, 215–27.

McNee reports a case that deserves special note, not only because of the rarity of the condition, but also because the author believes that it is only the second case in which the *Spironema pallidum* was demonstrated in the lesion.

After a revision of the history of syphilis of the stomach as recorded in the literature, the author gives the following classification of the varieties of gastric syphilis (Wile's).

I. **Gastric syphilis:**
- (*a*) Syphilitic catarrh.
- (*b*) Syphilitic round ulcer.
- (*c*) Diffuse syphilitic infiltration of the gastric mucosa, with distortion of the stomach.
- (*d*) Pyloric syphilis—including ulcer, cicatrix, gumma, and diffuse infiltration.

II. **Perigastric syphilis** (with secondary implication of the stomach).

All writers are agreed that the commonest form is a submucous gumma which breaks down into an ulcer, and is often treated as a carcinoma, the surgeon being misled by the palpable tumour, the cachexia and loss of weight, and the character of the gastric contents. Other varieties must be very rare. McNee's case, like many other recorded cases, showed a complete absence of hydrochloric acid and the presence of lactic acid.

McNee's patient, a man of 57 years, was in University College Hospital under Dr. Sidney Martin. He complained of pain in chest and abdomen, constipation alternating with diarrhoea, paleness, and loss of four stones in

weight in six months. A hard, irregular mass, of the size of a hen's egg, could be felt, moving with respiration, below the left costal margin. Free HCl was absent, lactic acid present. A diagnosis of malignant disease was made. Two severe attacks of haematemesis occurred, and symptoms of perforation were present. A Wassermann test was not made.

At autopsy a large, irregularly-shaped ulcer occupied about three-fifths of the stomach, especially involving the lesser curvature. The borders were greatly thickened, the floor bare, the margins covered with shaggy shreds of necrotic tissue, mixed with tenacious mucus. Except where two perforations were present on the posterior surface, the wall of the stomach was considerably thickened and had a dense pearly-white appearance similar to that seen in scirrhous carcinoma.

Microscopic examination showed almost all the stages between an active granuloma and a zone of scar tissue near the centre. Great numbers of *Spironema pallidum* were found.

The article is illustrated and has a bibliography; it is of especial interest in view of Dr. Monod's recent lecture at the Royal Society of Medicine. C. C. C.

Duval, P., et **Basset, A.** Coexistence d'une sténose de la troisième portion du duodénum par compression mésentérique et d'un ulcère de la première ou deuxième portion. [**Association of stenosis of the third part of the duodenum by mesenteric compression with ulcer of the first or second part.**] *Bull. et mém. Soc. de chir. de Par.*, 1922, **48**, 391–403.

Although the condition discussed by Duval and Basset is a rare one, the varieties of operative procedure by which it can successfully be treated are so strictly limited that a clear conception of the limits is imperative. Five cases are quoted from the literature, and one is added by the authors.

Logical treatment involves gastro-jejunostomy for the duodenal ulcer and duodeno-jejunostomy for the duodenal stenosis. Combination of the two operations without division of the jejunum involves forcing the latter to take a dangerously tortuous course, and necessitates a long loop with its attendant risks. The objection gains in force when the duodeno-jejunal anastomosis has to be made above the transverse mesocolon. The suggestion is made that, in cases where the duodenal ulcer is small and situated on the anterior wall near the pylorus, excision of the ulcer and pyloroplasty should be combined with duodeno-jejunostomy. When the duodenal ulcer is of a type which cannot be dealt with by pyloroplasty, a standard gastro-enterostomy combined with duodeno-jejunostomy is advised. The technique of the duodeno-jejunal anastomosis will then depend upon the area of duodenum exposed in the angle between mesentery and mesocolon. If this area is sufficient, a lateral anastomosis can be made. If not, the jejunum is divided, its distal end implanted into the duodenum either below or through the mesocolon, and its proximal end joined to the side of the distal segment. E. K. M.

Melanotte, M. La costante ureosecretoria di Ambard. [**Ambard's constant.**] *Arch. ital. di chir.*, 1922, **5**, 150.

This candid paper, based on more than 400 clinical investigations besides other research, while it may be said to damn the method with faint praise, discusses the many possible fallacies of technique and interpretation that surround it and similar tests. After a lucid account of the theory of Ambard

and an explanation of its terms and standards, the author points out that whilst K is a precise indication of the urea-secreting capacity of renal substance it may be lowered materially by fever; is usually low in diabetes where the total kidney substance is increased; is unreliable as to standard in nephritic dropsy or hydraemia; is raised in value by general anaesthesia, particularly by chloroform; is affected by pregnancy; and finally that the mere performance of ureteral catheterization may result in a K of unreliable magnitude for as much as ten days thereafter.

It is to be remembered that K gives no indication of the site of secreting parenchyma: it may be massed in one healthy kidney or diffusely scattered throughout both partly diseased organs. Where there is but one kidney and that not yet in compensatory hypertrophy, K may be 0·100, as against a normal 0·070; with one-quarter the amount of normal kidney substance K is 0·150; with one-eighth kidney substance normal K is 0·200.

The technique, with special apparatus used by the author, is described. He discusses the value of K in estimating a patient's capacity to withstand nephrectomy, and to withstand any operation calculated to put strain on his organic resistance. He considers those with diseased kidneys good risks up to K 0·100 (normal K 0·070); doubtful, K from 0·100 to 0·120; bad, above that, and particularly if above 0·150. With other than urinary disease, K is good up to 0·120, doubtful from 0·120 to 0·150, bad above that.

In estimating K it is necessary to consider the relative parts played by the primary kidney lesion and the secondary or associated nephritis; the latter is susceptible of amelioration by a régime, diet, rest, catheterization, but also by actual removal of the primary lesion where it is a cause of toxic nephritis.

Some kidneys can eliminate ample urea in low concentration, but the advent of oliguria may prove fatal. Azotaemia at 5 to 6 per thousand proves insupportable unless diuresis can be established.

All prostatics are to be regarded as potential uraemics. K is nearly always above normal, and though, of course, not the only guide, may be very valuable in indicating the necessity for two-stage operation.

In the case of renal lesions it must be borne in mind that K gives no indication of the site of competent substance. Where it is possible to establish the healthy state of one kidney by proof of excretion of urea, chlorides, indigo-carmine and water—in urine obtained by ureteral catheterization—estimation of K may be superfluous, and, if estimated, may be above 0·100 or even as much as 0·125, and yet be safe.

Where there is doubt about the efficiency of the 'good' kidney, whether because ureteral catheterization be impossible, or because palpation, exploratory lumbotomy, or other means suggest bilateral lesions, K may be of great value; for any figure above 0·120 spells danger. It may then be possible to perform a minor operation to rid the 'good' kidney of the toxic influence of the 'bad' one. In that case, if in spite of nephrotomy, with subsequent rest and dieting, K remains above 0·120, it would be unwise to proceed to nephrectomy and imperative to bear in mind the danger of fever, shock, and general anaesthesia. The author discusses various anomalous cases, where K 'good' did not avert a fatality, or conversely where operation in the face of a menacing K was followed by a happy result.

The impression left is that the problem has too many variables. It may be left with the author to characterize Ambard's constant as a sentinel of the zone of danger. E. R. C.

Randall, A., Small, J. C., and **Beek, W. P. Granuloma inguinale.** *Surg. Gynec. & Obst.*, 1922, **34**, 717–39.

Having had their attention drawn to this disease by the report by Symmers and Frost of two cases from the Bellevue Hospital, New York, the authors were startled to find that there were at that time seven cases in the Philadelphia General Hospital under wrong diagnoses.

To the abstractor's knowledge cases of this disease are sometimes to be seen in London hospitals amongst patients who have come from some of our tropical and semi-tropical dependencies; they are only occasionally correctly diagnosed and are found in surgical, genito-urinary, and venereal departments under various diagnoses, such as chancroid, tertiary syphilis, tuberculosis cutis, &c. It therefore seems justifiable to draw attention to this article.

The authors find that the disease is more widely spread through the United States than is usually recognized. Beginning as a small non-inflammatory papule which ruptures and refuses to heal, it slowly proliferates until the well-developed lesion shows itself as a flesh-red, exuberant, soft overgrowth of granulation tissue. True ulceration is not present in a typical case; the redundant edges overlap the surrounding healthy skin. Exudate is scanty, mucoid, non-offensive, and can be readily wiped off the underlying red, clean, bleeding granulations. The lesion may heal in the older parts, whilst spreading elsewhere. If secondary infection with pyogenetic organisms takes place, true pus, perhaps offensive in odour, and actual ulceration may occur.

The disease is especially localized in the groin, perinaeum, internatal cleft, and buttocks, and sometimes on the prepuce and labia; it may spread into rectum and vagina.

The authors' patients were negroes, except one, who was a white male. (The abstractor has seen the disease in a Chinaman.) A characteristic encapsulated bacillus originally described by Donovan is easily found in smears and is claimed to be pathognomonic, but it has not been cultivated until now. The authors have, however, succeeded in growing an encapsulated bacillus of the *Bacillus mucosus capsulatus* type; cutaneous inoculation into mice, guinea-pigs, rabbits, cats, and dogs failed to produce characteristic lesions; subcutaneous inoculations into the other animals used also failed, but in rabbits produced focal lesions, which, however, were not the characteristic granulomas seen in man.

The authors discuss the bacteriological methods fully, and describe the histopathology.

Local applications, vaccines, and arsenic are useless; excision is followed by recurrence. X-ray treatment does good, and slowly causes cicatrization (it completed cure in one case of the abstractor).

The authors obtained rapid healing with intravenous injection of antimony preparations, such as tartar emetic and sodium antimony thioglycollate. Sixteen cases are reported fully. C. C. C.

Howe, H. S. Normal and abnormal variations of the pituitary fossa. *Neurological Bulletin of the Columbia University*, 1919, **2**, 233–8.

Howe has measured and made tracings of the pituitary fossae of forty normal skulls and has found that this fossa is normally subject to great variations both in size and outline. Radiograms therefore give no information

of the condition of the pituitary gland unless the sellar enlargement or the amount of absorption of the bone is very great. He figures normal fossae showing all degrees of openness, of depth, and of width.

He points out that although the anterior clinoid processes, as seen on an X-ray plate, seem to form the anterior portion of the sella, this is an artefact of projection; the true anterior superior boundary is the tuberculum sellae. In acromegaly there may be (1) no change in the size or outline of the sella; (2) general enlargement of the sellar space without erosion or absorption of bone; or (3) enlargement with absorption of all or part of the bony envelope.

The normal hypophysis about fills the pituitary fossa transversely but not anteroposteriorly, so that there is room for some enlargement, by pressure on the circular venous sinus, before the bony cavity is filled.

It is frequently found in acromegaly that the fossa has been enlarged by the absorption of bone. The floor of the sella or its anterior or posterior wall is affected before the tips of the posterior clinoid processes or the top of the dorsum sellae. Supra-tentorial tumours and conditions causing chronic increase of intracranial pressure may induce absorption of the posterior clinoid processes. C. C. C.

Veau, V., et **Lascombe, J.** Traitement du bec-de-lièvre bilatéral complexe. [**Treatment of bilateral hare-lip.**] *J. de Chir.*, 1922, **19**, 113–36.

In the earlier cases of their series the authors were in the habit of operating at the age of 14–16 months. Since finding that, out of 11 cases observed at birth, only one returned for operation at the selected age, they have altered their views and now commence the reconstruction of the lip at 4 weeks. The operation is carried out in two stages, the first of which consists in reposition of the premaxillary process and temporary reconstruction of the lip, the definitive modelling of the latter being undertaken immediately before the eruption of the first dentition.

Stage I. Replacement of the premaxillary tubercle. This is never removed under any conditions, but is replaced by a process of sliding bodily backwards, not by rotating on a hinge. Cuneiform resection of a portion of the vomer is condemned on account of the depression of the tip of the nose which results.

A midline incision, commencing 1 cm. behind the line of the teeth and running back for 2 cm., is carried through the mucoperiosteum down to the bone. Mucoperiosteal flaps are separated from the vomer and the separation is carried as far as possible forwards towards the tip of the nose. The bony pedicle is then cut through, the tubercle turned up, and the upper pole of the intermaxillary bone removed until the whole process can be slid back into position between the maxillae. After freshening the opposed mucous surfaces, the tubercle is fixed to one or both maxillae by wire sutures and the upper lip reformed without any attempt to make it perfect. This step is of importance in counterbalancing the pressure of the tongue on the lingual aspect of the intermaxillary tubercle. The alae of the nose are freed and adjusted at the same time and fixed by a wire suture passing up through the lip 1 cm. from the cleft, through the ala, across the base of the premaxilla, and out on the other side through a corresponding track.

Stage II. The reformation of a lip involves consideration of three factors, skin, muscle, and mucous membrane. Manipulation of the skin is easy, and approximately equivalent results can be obtained by a large

variety of incisions. Reconstitution of the orbicularis is an essential step towards the future mobility of the lip. The handling of the mucous membrane is difficult because no part of it can be sacrificed without a risk of shortening and flattening of the lip.

The authors therefore commence with a horizontal incision across the premaxillary tubercle immediately above the muco-cutaneous junction. This incision divides skin alone and enables a flap of mucous membrane to be lifted from the lower border and posterior surface of the premaxillary tubercle. The usual skin incisions freshening the edges of the cleft are then made and the orbicularis reconstituted by fine, buried sutures of catgut. The skin edges are brought together and the flap of mucous membrane from the premaxilla used to fill up the V-shaped gap on the back of the lip.

E. K. M.

Bubis, J. L., and **Swanbeck, C. E. Gas cysts of the intestines.** *Ann. Surg.*, 1922, **75**, 620–5.

Bubis and Swanbeck record a case and give a short review of this condition, which is also known by the names pneumatosis, cystic pneumatosis, cystoides intestinis hominis, and emphysema of bowel. Although well-known in pigs, the condition is rare in man, and Weil only found reports of 70 cases.

Aetiology. Gas collects in one or more coats of the gut. Five theories have been propounded as to its mechanism.

(*a*) That the gas is due to putrefaction in certain cells. But Karsner points out that in such case bacteria should be found; most authors have failed to find any bacteria. Koskow stated that the giant cells show no vacuolation.

(*b*) That the gas is liberated from the tissue lymphatics. There is no positive evidence of this process.

(*c*) Bacterial origin—but bacteria and round-celled inflammatory infiltration are seldom found. Nitch believes that there is infection of the caecal wall with gas-producing organisms, and his case presented histological evidence that this had occurred. Moreover, in a few cases gas-forming organisms have been found by various authors.

(*d*) Neoplastic theory—but the condition rarely accompanies cancer and in most cases the cysts disappear.

(*e*) Mechanical theory—tuberculosis, appendicitis, &c., cause defects in the intestinal wall, which may be small and may be overlooked; then peristalsis increases the pressure on a column of gas in the lumen and forces gas through these paths of least resistance (Karsner).

The following associated lesions have been found: gastric or pyloric ulcer in 32 cases, intestinal tuberculosis in 4, pulmonary tuberculosis in 2, appendicitis in 2, chronic enteritis in 2.

The authors record a case in which there was an ulcer at the base of the appendix. The history included weakness, malaise, pain in right side of the abdomen, radiating to the right testis. No vomiting or nausea. Urinary frequency at night. 15 lbs. weight lost in 4 months. Examination revealed a sausage-shaped boggy tumour in the right lower quadrant of the abdomen; it was tender, and very freely movable, especially upwards. At operation the caecum, appendix, and ascending colon were found to be thickened, contracted, oedematous, doughy, and crepitant; minute gas cysts

were seen under the serosa. Removal of the mass and intestinal anastomosis led to recovery.

The gas cysts were found through all coats of the thickened gut wall, especially in the mucosa and submucosa. The cysts were lined with endothelium; many giant cells were seen, but no pus cells. No bacteria and no inflammatory reaction were found.

Mere exploration sometimes cures the condition in a remarkable manner (Weil), but excision of the affected part is advisable. C. C. C.

Nitch, C. A. R., and Shattock, S. G. Diffuse emphysema of the intestinal wall (two cases) with remarks upon pneumatoses. *Proc. Roy. Soc. Med.*, 1919, **12** (Surg. Sect.), 46–86.

In a full, illustrated article Nitch and Shattock describe two cases of intestinal pneumatosis operated upon by Nitch. They discuss fully the general subject of pneumatosis as it affects serous cavities, connective tissue, alimentary and genito-urinary tracts, and then devote their attention particularly to the intestine.

As regards pathogenesis various theories, such as secretion of the gas, liberation of the gas from the tissue lymph, mechanical causation, bacterial origin, are discussed, and the authors sum up the evidence in the first case as slightly in favour of mechanical causation. This patient had pyloric stenosis with greatly dilated stomach; in the part removed for microscopical examination no bacteria were seen and there was a complete absence of the small round-celled infiltration that was so conspicuous in the second case. In this latter they believe that the histological picture was that of a somewhat acute infective process involving not only the submucosa, but, in places, also the muscularis.

After referring to the literature (see Shennan, T., and Wilkie, D. P. D., *J. Path. and Bacteriol.*, 1910, **14**, 259) the authors state that the pathogenesis of each case needs discussion on its own merits. The emphysema is due:

(*a*) In some to trauma by over-distension of the mucosa, the gas being derived from the intestinal lumen, augmented perhaps by some produced locally by secondary infection.

(*b*) In others, to local bacterial infection, associated, or not, with an ulcer.

(*c*) In others, to forcible introduction of gas from the lumen through an ulcer.

The collection of gas is essentially in the submucosa, but shows through the peritoneal coat as blebs. In the first case the condition was found accidentally and affected the whole small intestine except duodenum in a man who had a pyloric stenosis with gastric symptoms of some years' standing. The second case was in a woman of 40 who had obscure abdominal symptoms with normal pulse and temperature. She had been attacked with acute colic in the right iliac fossa 12 days previously; the pain subsided, but recurred a week later. At operation the walls of caecum and ascending colon were thickened, inflamed, crepitant, and beads of gas were seen in neighbouring epiploicae; the small intestine and vermiform appendix were free.

In the first case recovery followed gastro-enterostomy; in the second it followed resection of caecum, ascending colon, and part of transverse colon.

C. C. C.

McNee, J. W. The use of the Van den Bergh test in the differentiation of obstructive from other types of jaundice. *Brit. M. J.*, 1922, i, 716.

McNee shortly describes Van den Bergh's test and its uses, and believes that it fully reaches expectations.

Van den Bergh's test for the presence of bile-pigment (bilirubin) in the blood-serum was first described in 1913, and fully discussed in his monograph 'Der Gallenfarbstoff im Blute' in 1918. In 1921 Lepehne and also Rosenthal and Holzer confirmed some of Van den Bergh's results.

McNee, in a few cases, has confirmed the value of the test as distinguishing the obstructive from the haematogenous and the hepatogenous types of jaundice. In the latter category he places the various forms of haemolytic and acholuric jaundice and also functional jaundice such as catarrhal jaundice, toxic jaundice in infective disease, icterus neonatorum, &c. It will be noted that he regards catarrhal jaundice as depending on a hepatitis with functional derangement of the liver and not on an obstruction of the bile-ducts.

Van den Bergh has applied the so-called 'diazo reaction', first described by Ehrlich, who found that bilirubin, when dissolved in chloroform or alcohol, gives with diazonium salts a reddish colour in neutral solutions and a bluish one in acid solutions.

Using this reaction, Van den Bergh and Snapper found that they could demonstrate the presence of bilirubin in serum with great delicacy. They found that every normal serum contains bilirubin in a solution of from 1 in 400,000 to 1 in 250,000. Biliverdin, lutein, &c., do not give the reaction, nor does any other substance found in human serum.

McNee describes the technique shortly.

One of three results may occur:

1. An Immediate (Direct) Reaction, beginning at once and maximal in ten to thirty seconds. The colour becomes bluish-violet.

2. A Delayed Reaction, beginning only after one to fifteen minutes or longer. The colour becomes reddish, which gradually deepens to a violet.

3. A Biphasic Reaction. In this a slight reddish colour appears immediately in ten to thirty seconds and a minute or two later deepens to a violet.

If the reaction is immediate or direct an obstructive jaundice is indicated.

If this is not obtained, the test is carried farther by an alcohol precipitation; if this is positive a violet-red colour reaching maximal intensity almost at once indicates the presence of bilirubin. When no direct reaction has been given, but a perfect indirect reaction occurs after alcohol precipitation, then the jaundice is probably haemolytic or hepatogenous.

The different reactions to the test in obstructive and in the other varieties of jaundice may be due, as Van den Bergh suggests, to the bilirubin, which only gives the indirect test, being bound in some way to albuminoid substances in the serum. On this assumption the biphasic reaction would be explained by the presence of both types of bilirubin in the serum simultaneously.

As the 'indirect' reaction, which is given by all forms of jaundice, can be quantitatively estimated colorimetrically, the test affords a satisfactory method of estimating the amount of bile-pigment in the serum.

If further examination confirms the test as a method of distinction between the truly obstructive jaundices and the other varieties, including

the catarrhal forms, and as a method of accurate estimation of the degree of jaundice, whether fading or deepening, it will probably prove of great practical value to the surgeon. C. C. C.

NEUROLOGY

Hallervorden u. Spatz. Eigenartige Erkrankung im extrapyramidal motorischen System. Ein Beitrag zu den Beziehungen zwischen Globus pallidus und Substantia nigra. [**Unusual lesion of the extrapyramidal motor system, with reference to the relationship between Globus pallidus and Substantia nigra.**] *Wissenschaftliche Sitzung der deutschen Forschunganstalt für Psychiatrie in München*, 1922, **22**, 2 ; *Zentralbl. f. d. ges. Neurol. u. Psychiat.*, 1922, **28**, 518.

The authors report the pathological examination of the brain in a case of congenital imbecility, with generalized flexor contractures and choreo-athetotic movements. The patient died at the age of 24. To the naked eye the brain was normal, except that the globus pallidus and substantia nigra on both sides were of a deep brown colour. Microscopically, they found diffuse nerve-cell and fibre changes throughout the brain. In addition, the following changes were found in the pigmented structures named above, and minutely confined to them: thickly-scattered dark brown pigment granules (? within the nerve-cells), which gave an intense iron reaction, but no calcium reaction, and also a smaller number of almost colourless granules which did not contain iron; numerous large glia nuclei, which were not like those described by Alzheimer in pseudo-sclerosis.

The authors believe that this pigmentation is a pathological exaggeration of a condition normal to both globus pallidus and substantia nigra, but especially to the latter. It indicates a close physiological relationship between these structures. The pigment is a product of metabolism and they attribute its formation to the glia nuclei. They regard it not as haematogenous, but as autogenous. The blood-vessels were normal, and the nerve-cell changes were less marked in these ganglia than elsewhere in the brain.

They mention that the clinical picture observed during life corresponded to the pallidum syndrome of C. and O. Vogt. If the views of the Vogts be correct, this is what would have been expected, but it was not so, for choreo-athetotic movements are described as being present, one of many indications of the caution necessary in accepting the theoretical conclusions of these observers. The liver was not examined in this case, but the authors believe that it did not belong to the group progressive lenticular degeneration pseudo-sclerosis, but approximated to C. and O. Vogt's status dysmyelinatus. The possibility that lesions of the substantia nigra may play a more important part in the production of the so-called corpus striatum syndromes than is generally supposed is mentioned. F. M. R. W.

Sachs, B., and Friedman, E. D. General symptomatology and differential diagnosis of disseminated sclerosis. *Arch. Neurol. & Psychiat.*, 1922, **7**, 551.

Taylor, E. W. Multiple sclerosis: the location of lesions with respect to symptoms. *Arch. Neurol. & Psychiat.*, 1922, **7**, 561.

Bailey, Pearce. Incidence of multiple sclerosis in United States troops. *Arch. Neurol. & Psychiat.*, 1922, **7**, 561.

Friesner, I. **Lesions of the auditory and vestibular apparatus in multiple sclerosis.** *Arch. Neurol. & Psychiat.*, 1922, **7**, 584.

Hassin, G. B. **Studies in the pathogenesis of multiple sclerosis.** *Arch. Neurol. & Psychiat.*, 1922, **7**, 589.

Leiner, J. H. **An investigation of the axis cylinder in its relation to multiple sclerosis.** *Arch. Neurol. & Psychiat.*, 1922, **7**, 608.

Hassin, G. B., and **Bassoe, P.** **Multiple degenerative softening *versus* multiple sclerosis.** *Arch. Neurol. & Psychiat.*, 1922, **7**, 613.

Sanger Brown II and **Davis, T. K.** **The mental symptoms of multiple sclerosis.** *Arch. Neurol. & Psychiat.*, 1922, **7**, 629.

This number of the Archives is devoted to papers on the symptomatology and morbid anatomy of disseminated sclerosis. In a short introductory paper **Sachs and Friedman** give an analysis of the various symptoms observed in a series of 141 cases of the disease. (1) Easy fatigue, weakness, and stiffness of one or more limbs, culminating in spastic paraplegia, 81·7 per cent. (2) Nystagmus, 70 per cent. (3) Ataxic tremor of upper limbs and tremor of the head, 55·3 per cent. (4) Marked diminution or abolition of abdominal reflexes, 80 per cent. (5) Spastic ataxic or ataxic gait and stance including Rombergism, 43·2 per cent. (6) Some form of dysarthria, 36 per cent. (7) Pallor of optic disks, especially temporal halves, 32·6 per cent. (8) Disturbance in facial innervation, often slight, 32·6 per cent., with deviation of tongue in 10 per cent., and defect of deglutition in 3·5 per cent. (9) Explosive laughter and emotional instability, 17 per cent. (10) Unusual remissions, 42 per cent. (11) Transitory ocular palsies with diplopia, 29 per cent. (12) Vague objective and subjective sensory disturbances of posterior column type in 17, and pain, touch, and temperature in 16·3 per cent. Tingling and numbness in 30 per cent. (13) Bladder disturbances, 40 per cent. (14) Tenderness of dorsal spine, 12 per cent. (15) Vestibular vertigo, 8·25 per cent. (16) Mental changes, 15·6 per cent. (17) Auditory nerve symptoms, 2 per cent. On the negative side, normal pupillary reactions and negative cerebrospinal fluid examination (except for occasional cellular or globulin excess) were constant.

No single positive sign is constantly present in all cases, and diagnosis can be made on various combinations, although the triad, nystagmus, scanning speech, and intention tremor, may be absent.

Taylor discusses the correlation of the lesions with the clinically observed symptoms. Although the same principles of localization as are applied to other diseases of the nervous system are valid in the case of disseminated sclerosis, yet Taylor admits that an exact correlation is impossible to obtain. He quotes Brouwer's paper (cf. *Medical Science*, 1920, **2**, 271), in which this author suggests that the different parts of the central nervous system may differ in their vulnerability, the simplest and phylogenetically oldest functions being more resistant and less likely to give rise to symptoms of disorder when their anatomical basis is involved in a patch of the disease. This is a modern application of Jackson's theory of the evolution and dissolution of the nervous system, and is clearly a factor to be seriously considered in this connexion.

The most satisfactory correlation between lesion and symptoms has been established in the case of the optic nerves and tracts, and Taylor quotes

from Uhthoff in this connexion. Otherwise he has no new information or suggestions to offer, and the paper is a disappointing one.

Pearce Bailey gives statistics of disseminated sclerosis in the United States Army during the war period. The neurological authorities examined three and a half million recruits, finding 6,919 cases of organic nervous disease. These included 511 cases diagnosed as disseminated sclerosis (or 7·4 per cent.). He gives the racial incidence of the disease, but the table contains no striking information.

Friesner discusses lesions of the auditory and vestibular apparatus in ten cases. He believes that the nystagmus is attributable to a lesion involving oculo-vestibular paths. He found that it frequently persisted underlying a superimposed nystagmus induced by caloric stimulation, the two sometimes combining to produce bizarre movements of the eyes. Sometimes a skew deviation may be seen in these circumstances. None of the series showed vertigo, and, in four cases, even induced nystagmus was unaccompanied by vertigo.

Hassin describes the pathological lesions found in the nervous system of thirteen fatal cases. In all patches of sclerosis he finds apparently healthy nerve-fibres, fibres totally or partly de-myelinated and fibres in a state of Wallerian degeneration, both axis cylinder and myelin being in process of destruction. These changes are also found in parts of the central nervous system which show no visible patches. Between the diseased area and normal tissues is seen an intermediate zone, in which the axis cylinders are fairly well preserved, but occasionally swollen or fragmented. He believes that the earliest pathological change in the disease is in the myelin—a periaxial neuritis. This is accompanied by marked secondary proliferative changes in the glia tissue. The spaces between the swollen fibres are filled by glia fibres or by large glia nuclei, rich in chromatin, with abundant cytoplasm and a well-defined cell-membrane.

Some astrocytes with numerous branching processes are to be seen, and also myeloclasts, cells with granular broken-up bodies, an eccentric pyknotic nucleus, and lipoid droplets.

The blood-vessels and pia exhibit secondary changes, hyperplasia, and thickening, with dilatation of the perivascular spaces, which are filled with 'gitter' cells. In areas of longer standing, 'myelophages' are seen, which pick up degenerated nerve-tissue and transform it into lipoid droplets within their vacuoles. The 'gitter' cells contain these droplets in larger masses, and both gitter cells and myelophages represent a more advanced stage of degeneration than that in which myeloclasts occur. After the degenerated myelin and axis cylinders have been removed by cells of these three types, and taken up into the blood-vessels, the destroyed nervous elements are replaced by a glia tissue scar—the patch of sclerosis. This consists of densely-packed fine neuroglia fibres radiating from deeply-staining oval or rod-like nuclei. Large glia nuclei are also found. This represents the final stage in the development of a lesion. In striking contrast to the profound changes in nerve-fibres is the relative integrity of the nerve-cells, which show no change except some axonal reaction in severe lesions. The vessels show no inflammatory changes, nor any hyaline degeneration, but simply the hyperplastic phenomena described above. These various histological appearances are minutely described, together with the staining methods necessary to demonstrate them. Hassin concludes that the initial change is a widespread swelling of the myelin sheaths, developing acutely

and giving rise to the formation of a 'waxy patch'. The glia changes occur secondarily. The patches do not follow vascular distribution.

Leiner has studied the axis cylinder changes in disseminated sclerosis. He finds that the myelin sheath disintegration is accompanied by oedema of the axis cylinders, which may be damaged or destroyed, though they frequently survive. Of the two the myelin sheath is the more severely affected.

Hassin and Bassoe compare the lesions typical of disseminated sclerosis with those found by them in a case of 'multiple degenerative softening'. Examples of this condition are probably to be found in the cases described as degenerative encephalitis, disseminated encephalomyelitis, Wernicke's polioencephalitis superior, and various other conditions which do not conform to generally recognized morbid entities. The patient was a man of 28, who first came under treatment for a septic infection of the finger and was found to have tonsillitis, conjunctivitis, and other chronic infections. Some days after discharge from hospital, he returned complaining of headache, loss of vision, vertigo, and tinnitus, with hesitant micturition. He lived seven weeks, and before relapsing into stupor presented the following signs referable to the nervous system. Gross defect of vision without visible lesion of the fundus, deafness of the left ear, large unequal pupils which were sluggish to light, nystagmus, slight weakness of the left face and external rectus of the eye, and rigidity of the neck muscles. There was no definite paralysis, the reflexes varied from day to day, and there was some difficulty in micturition. The illness was afebrile except for a terminal pyrexia. Autopsy revealed, among other visceral lesions, broncho-pneumonia and pleurisy, fatty liver, fibroid kidneys, and arteriosclerosis. The fresh brain was normal in appearance to the naked eye, but later examination of the celloidin blocks revealed the presence of distinct, pale, sharply-defined areas resembling patches of disseminated sclerosis in brain-stem, cerebellum, and caudate nucleus. Histologically, however, the lesions differed fundamentally from those of disseminated sclerosis. The foci of disease were entirely lacking in nerve-cells and fibres, and consisted in a mass of cellular elements of glial origin, myelophages, and 'gitter cells'. The capillaries were thickened and numerous, and the perivascular spaces were packed with 'gitter' cells, which, like those in the rest of the lesion, were filled with lipoid material. Perivascular infiltration was widespread throughout the brain, the cells being principally 'gitter' cells, and not lymphocytes or plasma-cells.

In addition to the foci of total degeneration, there was diffuse nerve-cell degeneration throughout the cerebral hemispheres, chromatolysis, neuronophagia, and fatty change. Numerous rod-cells (Stäbchenzellen) were also seen throughout the brain. The spinal cord showed similar pathological phenomena. The authors compare their case with numerous recorded cases in the German literature which they believe to be similar in nature. They conclude that, apart from acute inflammatory brain lesions, acute degenerative lesions are common. They present varied and indefinite clinical symptoms, but the lesion is so characteristic that they believe it justifiable to group the cases under the heading of 'multiple degenerative softening'.

In a final paper, **Sanger Brown II and Davis** discuss the common mental changes in disseminated sclerosis. Euphoria is perhaps the commonest deviation from normal in this respect. In the great majority of

cases it does not amount to a psychosis, it is simply 'a marked inconsistency between the patient's mood and his physical disability'. Dementia is not common, even as a terminal state, but is seen from time to time and may then be serious. Associated with it may be delusions of grandeur comparable with those observed in general paralysis of the insane. Depression, with suicidal tendencies, is infrequent. Hallucinations of hearing without insight are not uncommon. Changes in the personality are rare. Like the physical symptoms, such mental manifestations as may occur tend to be transient and to be subject to remission. They divide mental symptoms in this disease into two groups: first, those which are the direct result of the organic lesion, including euphoria, mental deterioration, auditory hallucinations, certain rare cases of Korsakow psychosis, and delusions of grandeur. In a second group they include those which are 'incidental and secondary', transitory delusional and depressed states, symptoms suggestive of dementia praecox. This group is attributed to that inherent state known to American writers as the 'mental make-up' of the patient.

F. M. R. W.

Carter, H. S. On causalgia and allied painful conditions due to lesions of peripheral nerves. *J. Neurol. & Psychopathol.*, 1922, **3**, 1.

The paper is based upon the examination of over a thousand cases of peripheral nerve injury. The author describes causalgia as an intensely painful condition almost entirely limited to certain sensory areas of the median and sciatic nerve distributions, and caused by lesions of these nerves at points more or less distant from these areas. It is characterized by local vasomotor disturbances and general hypersensitiveness of the nervous system. In short, a painful vasomotor neurosis due to irritation of a mixed nerve. He gives an historical *résumé* of the history of knowledge on the subject. Four clinical varieties of the condition are described.

(i) **The syndrome of slight nerve irritation,** in which there is little or no pain when the limb is at rest. In the cutaneous distribution of the affected nerve there is qualitative sensory change, but no trophic lesions, no contracture, and but slight impairment of function. Recovery is generally rapid.

(ii) **The syndrome of irritation of mild neuralgic character.** Here the pain is of aching character along the course of the nerve and at the site of injury. There are slight qualitative sensory changes, and in other respects the cases resemble those in group (i).

(iii) **The syndrome of severe nerve irritation.** This is found in the case of mixed nerves containing numerous vasomotor and 'trophic' fibres. Pain is prominent and is intensified by heat and cold. There is cutaneous hyperaesthesia, and sometimes hypaesthesia to cotton wool touch in the distribution of the nerve. There are marked trophic lesions and gross defect of function.

(iv) **The syndrome of irritation of severe neuralgic nature** characterized by intense aching pain along the course of the nerve. In all the cases examined some type of causalgia was present in 1 in 130, and so-called major causalgia in 1 in 750. Only one civil case is included in the series, and it is somewhat doubtful whether it belongs there. The nerve lesion is said to have been 'gouty deposits' in the nerve-trunk, and the symptoms and clinical course correspond to the ascending neuritis of continental writers.

The clinical picture. Pain is the dominant feature, and is burning in character and intense. It is aggravated by moist or dry heat, but may be relieved by cold moisture, such as may be provided by the use of an evaporating lotion. In the case of the median nerve, the pain is commonly localized to an area of skin bounded by the root of the thumb, the base of the index and second fingers, and by a line drawn down the middle of the palm. In the case of the sciatic it is found over the middle third of the inner half of the sole. Movement of the limb, peripheral and emotional stimuli, all aggravate the pain. The patients rapidly develop emotional instability and tend to immobilize the affected part. Such objective sensory loss as is present is slight, but the details as to the form it takes are not very clear. On the motor side, there is slight weakness and wasting of the muscles supplied by the affected nerve. Vasomotor disturbances are constant, there is local vaso-dilatation and rise of skin temperature, and commonly also excessive sweat secretion. The skin is glossy, reddish, mottled, and thin, and the nails are curved and grooved. The tendon-jerks in the affected limb are commonly increased. Apart from treatment, all but the slightest cases tend to progress. Wasting of muscles and contracture and increasing trophic lesions of the skin and nails occur.

The incidence of causalgia is selective, and the nerves commonly involved are the median and sciatic trunks, or the nerve-roots entering into the median nerve, or the internal popliteal and posterior tibial nerves. In discussing the explanation of this peculiarity, Carter points out that both sciatic and median nerves supply specialized areas of skin, the sole and the palm respectively. Both are associated with various forms of receptor organ in the skin. Both carry numerous vasomotor and trophic fibres for the skin, and both possess a large accompanying artery and are in their course associated with the large arteries of the limbs. Beyond stating these factors of possible significance, the question is not discussed.

In discussing **the origin of the symptoms** Carter is not very clear. He rejects the view that either paralysis of vasoconstrictor or irritation of vasodilator fibres is responsible, and believes that the symptoms are reflex in origin, and arise from irritation of fibres of depressor function at the site of the lesion. This gives rise to afferent stimuli, which are reflected from spinal centres downwards in vasodilator fibres as 'antidromic impulses'. Apparently, one of his main reasons for this belief is Mackenzie's dictum that symptoms are manifestations of disturbed reflexes. Were any refutation of so specious and inaccurate a generalization needed, Carter himself supplies it, when he observes that section of the injured nerve above the level of the lesion does not abolish the symptoms, though it necessarily interrupts the reflex arc. He believes that two factors are active in producing causalgia, damage to the sheath of the nerve, with extravasation of blood into the nerve, and subsequent organization and fibrosis, and, secondly, bruising of a nerve by the passage of a projectile through adjacent tissue, with extravasation of blood and changes like those mentioned above. The microscopic lesion is an intraneural and perineural sclerosis of the nerve-trunk.

Treatment. Surgical procedures have to be delayed until fear of complicating sepsis is past. During this period, and for slight cases, some relief is obtainable by the use of evaporating lotions and sedative drugs. In severe cases, surgical treatment is alone effective. He has found neurolysis useless, and recommends excision of the injured length of nerve, with

end-to-end suture. He is not in favour of alcohol injections into the nerve, nor of Leriche's 'peri-arterial sympathectomy'. After operation, ionization of the scar with 1 per cent. sodium chloride solution, combined with massage and mild electrical stimulation of the paretic muscles, passive movements, and re-education exercises are indicated.

The objective sensory changes commonly found are described, and a tabular list of cases of major and minor degrees of causalgia is added as an appendix. Finally, a diagram illustrating the writer's method of recording results, and a series of photographs, conclude an interesting and valuable paper. F. M. R. W.

PATHOLOGY AND BACTERIOLOGY

Burke, V. Notes on the Gram stain with description of a new method. *J. Bact.*, 1922, **7**, 159.

This is a study of the factors involved in the Gram staining process. The author finds that there are, in particular, two critical steps in Gram's method, viz. (*a*) the removal of water after the iodide solution, and (*b*) the decolorization, the control of these determining to a large extent the amount of differentiation between Gram + and Gram − micro-organisms. If films become dry after the application of iodine the Gram − microbes retain the dye much longer. Acetone was found preferable to alcohol as a decolorizing agent reducing the time required for the decolorizing process and giving a greater time period between the decolorization of Gram + and Gram − bacteria. The author describes a modified Gram method which he has devised. In detail, the film is spread thinly, air dried, and fixed with the least amount of heat necessary to kill the bacteria and fix them on the slide. An aqueous 1 per cent. solution of dye is employed and to it are added on the slide 3 to 8 drops of a 5 per cent. solution of sodium bicarbonate. Stain for two to three minutes. Flush off the excess stain with iodine solution (I 1 gm., KI 2 gm., distilled water 100 c.cm.) and cover with fresh iodine solution for one minute or longer. Wash in water and blot off all excess of water until the surface of the film is practically water-free. The film, however, should not be allowed to become dry. Decolorize with acetone or acetone-ether (3 : 1) until the decolorizer flows from the slide practically uncoloured (about 10 seconds being required). Blot dry. Counter-stain for 5 or 10 seconds in a 2 per cent. aqueous solution of safranin O. Wash off excess of stain, blot and dry. Immerse in xylol or turpentine. Mount. W. B.

Petriccioni, E. Sugli streptococchi della bocca e loro rapporto con le polmoniti post-operatorie. [**On streptococci of the oral cavity and their relation to post-operative pneumonias.**] *Ann. d'ig.*, 1921, **31**, 688.

A non-haemolytic streptococcus of the type *S. buccalis* Blake was isolated from the oral cavity of 50 per cent. of the 26 normal subjects investigated, the haemolytic streptococcus in three of them, and in two out of three patients suffering from post-operative pneumonia. C. d. F.

Sacchetto, J., e **Savini, M.** Ricerche su una varietà di setticemia del coniglio. [**Investigations on a form of rabbit-septicaemia.**] *Boll. d. Ist. sieroter. Milanese*, 1921–2, **2**, 217.

During an epizootic among the rabbits of the Padua Institute of General Pathology, the authors were able to isolate a coccobacillus similar to the well-known ovoid form of rabbits' septicaemia (pasteurella of French authors). The coccobacillus of Sacchetto and Savini causes in rabbits a septicaemia, but this is characterized by very scanty macroscopic lesions and by the absence of haemorrhages. For this reason, and for the morphological and cultural characteristics of their coccobacillus, the authors think that it is a species not as yet described. C. d. F.

Burnet, E. Sur un nouveau procédé de diagnostic de la fièvre méditerranéenne. [**A new method of diagnosing Malta fever.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 421.

An intradermal injection of a drop of the filtrate of a month-old broth culture of *Micrococcus melitensis* produces a characteristic lesion in patients suffering from Malta fever, and for a period extending up to 5 months after recovery. A positive reaction consists in the appearance, 7 hours after the injection, or later, of a small patch of oedema with or without a little redness and pain. The patch varies from 4 to 6 c.cm. in diameter, and has a sharply defined and regular edge. It is best seen 24 hours after the injection and lasts several days. The filtrate can be preserved quite safely by the addition of 0·5 per cent. of phenol. The reaction is specific, as normal individuals and patients suffering from tuberculosis, typhoid fever, and malaria gave negative reactions. J. R. P.

Olitsky, P., and **Gates, F. L.** **Experimental studies of the nasopharyngeal secretions from influenza patients. VII. Serological reactions.** *J. Exper. M.*, 1922, **35**, 553.

The previous researches of the authors have been abstracted in *Medical Science* (1921, **4**, 266; 1921, **5**, 62). An anaerobic filter-passing bacilloid microbe, *B. pneumosintes*, was found in the naso-pharyngeal secretions of patients suffering from uncomplicated influenza and also from the lungs of rabbits and guinea-pigs inoculated with such secretions. In the present communication they report that they have succeeded in obtaining good growths of the microbe in a collodium sac dialysate of the medium of Smith and Noguchi. The growth so obtained was found to possess antigenic properties causing the appearance of agglutinins, precipitins, complement fixation, and phagocytic reactions. Four different strains of *B. pneumosintes* were found to be identical. W. B.

Léger, M., et **Baury, A.** La musaraigne, Crocidura Stampflii, et la peste au Sénégal. [**The shrewmouse, *Crocidura stampflii*, in relation to plague in Senegal.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 423.

Contrary to the findings of British observers in India, the authors find that the shrewmouse is a carrier of *B. pestis* in Senegal, as many as 9·37 per cent. being found infected in comparison with 10·8 per cent. of rats in the same locality. The only flea which was found on the shrewmouse was *Xenopsylla* (*Pulex*) *cheopis*. As the shrewmouse does not wander far from its usual foraging ground, it is not so dangerous as the rat, but it can act as a reservoir of the disease, which tends to run a more chronic course in this animal than in the rat. J. R. P.

Kendall, A. I., Day, A. A., and **Walker, A. W.** **Metabolism of *B. welchii, Vibrion septique, B. fallax, B. tertius, B. tetani, B. pseudotetani, B. botulinus, B. bifermentans, B. oedematiens, B. aerofoetidus, B. sporogenes, B. histolyticus,* and *B. putrificus.*** *J. Infect. Dis.*, 1922, **30**, 141.

This paper deals with exact chemical studies which have been carried out on cultures of the principal anaerobic bacteria associated with war wounds. The methods were mainly those employed by Wolff and his collaborators in similar studies, and included the change in titrable acidity, the measurement of changes in the nitrogenous constituents of the media—ammonia formation, amino-acid liberation and utilization—the total nitrogen content, and attempts to demonstrate proteolytic enzymes. The cultures intended for study were grown in special flasks and a separate one was inoculated for each kind of medium for each day of observation. The authors believe that this method far exceeds in accuracy the alternate plan of removing samples at stated intervals from the same flask. Various strains of each microbe were tested and the results are set out in elaborate tables. These results confirm in most respects those of Wolff and Harris, and of the Anaerobic Committee of the M.R.C., but must be studied in detail by those specially interested. W. B.

Uhlenhuth, P., u. **Hailer, E.** Über die Desinfektion mit tuberkulösem Auswurf infizierter Wäsche. [**The disinfection of linen soiled by tuberculous sputum.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 208–13.

Uhlenhuth and Hailer have found that the disinfection of linen on which tuberculous sputum has dried is far easier than the sterilization of whole sputum. A 3 per cent. solution of alkali-lysol or parol disinfected linen in 2 to 4 hours, and a 2 per cent. aqueous solution of kresol in 1 hour. Further research is still required in order that a process may be evolved which assures the minimum injury by chemicals to the linen and is yet effective in destroying tubercle bacilli. C. L.

Stubbe, H. Die Wildbolzsche Eigenharnreaktion. [**The Wildbolz auto-urine reaction.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 265–70.

Stubbe, who has carried out the Wildbolz test in about 100 cases at Brauer's hospital in Hamburg, summarizes his findings thus: (1) in active tuberculosis the urine is flooded with specific antigens; (2) the test is specific for tuberculosis; (3) it is indicative of activity of disease, for the reaction becomes definitely weaker as recovery sets in, and is negative in the non-tuberculous, who give a positive tuberculin reaction; (4) the test provokes no general or focal reaction, and in this respect it is superior to the tuberculin test. Stubbe emphasizes the difficulties and tediousness of the technique. C. L.

Landgraf, T. Über den Wert der Wildbolzschen Eigenharnreaktion für den Nachweis der Tuberkulose. [**The value of the Wildbolz auto-urine test for tuberculosis.**] *Beitr. z. Klin. d. Tuberk.*, 1922, **50**, 258–61.

Landgraf has tested more than 100 cases of pulmonary disease with the Wildbolz auto-urine reaction at the Communal Tuberculosis Hospital in Hanover. He obtained a positive reaction in 90 per cent. of the cases of open pulmonary tuberculosis, in 80 per cent. of closed pulmonary tuberculosis, and in 44 per cent. of the cases in which the clinical diagnosis of pulmonary tuberculosis was in doubt. The reaction was invariably negative

in cases of non-tuberculous pulmonary disease. He concludes that the test is almost invariably positive in the presence of definite tuberculosis. In non-tuberculous persons the test is always negative, but the difficulties of treating the urine, inoculating the antigen, and interpreting the reaction are so great that the test should be confined to institutions. C. L.

Galassi, C. Ricerche e considerazioni sulla urino-reazione alla Wildbolz. [**Investigations on Wildbolz's auto-urine reaction.**] *Boll. d. Soc. med.-chir. di Pavia*, 1921, **34**, 41.

Reference has already been made to Wildbolz's auto-urine reaction for the demonstration of active tuberculosis (*Medical Science*, 1921–22, **5**, 559). According to Galassi the reaction is in some cases such as to suggest that it may be due to the presence in the urine 'of something unknown'. Apart from this fact the reaction appears to be insufficiently well-defined and constant to be of any practical value both from diagnostic and prognostic points of view. C. d. F.

Pestalozza, L. Contributo allo studio sperimentale della tubercolosi nei vertebrati eterotermi. [**Contribution to the experimental study of tuberculosis of cold-blooded vertebrates.**] *Boll. d. Ist. sieroterap. Milanese*, 1921–2, **2**, 223.

Tubercle bacilli of human and avian tuberculosis do not grow in tissues of cold-blooded animals, and after a time they disappear without causing any reaction on the part of the host. During the process of destruction human and avian tubercle bacilli lose their acid-fast characteristics in a way similar to that recently described by Métalniknow (*La Nature*, 1921, **49**, 212). The bacilli of bovine tuberculosis when injected into the muscles of the tench or administered *per os* to the same animal multiply particularly in the liver, but without causing any tissue reaction. When thus vegetating in the tench, bovine tubercle bacilli acquire the characteristics proper to bacilli of cold-blooded animals. C. d. F.

Sanfelice, F. La tubercolosi degli animali a sangue freddo. [**The tuberculosis of cold-blooded animals.**] *Boll. d. Ist. sieroter. Milanese*, 1921–2, **2**, 199.

Tubercle bacilli of mammalian origin are not pathogenic for reptiles and amphibia, but remain alive and virulent in their organs for very long periods. In the organs of reptiles and amphibia inoculated with tubercle bacilli from tuberculous mammals, acid-fast bacilli and an acid-fast streptothrix are constantly found. A similar finding in non-inoculated amphibia and reptiles is exceptional. It has not, as yet, been possible to ascertain whether such acid-fast bacilli and streptothrix may be transformed into tubercle bacilli of cold-blooded animals. C. d. F.

Botti, A. Il metodo di Konrich per la colorazione del bacillo di Koch. [**Konrich's method for staining Koch's bacillus.**] *Gazz. d. osp.*, 1921, **42**, 538.

Vascellari, G. Sulla colorazione dei bacilli tubercolari col metodo Konrich. [**On the staining of tubercle bacilli by Konrich's method.**] *Gazz. d. osp.*, 1921, **42**, 660.

Vascellari's investigations were made by the original method of Konrich (*Deutsche med. Wchnschr.*, 1920, **46**, 741), while Botti had resort to two French modifications (*Presse méd.*, 1921, **29**, 5) termed quick and slow

processes. The authors reached the same conclusion, viz. that the results obtainable by Konrich's method are, both in the case of smears and in that of sections, more certain and plainer than those attainable by the usual Ziehl-Neelsen process. In addition, Konrich's method has the advantage of economy, no alcohol being required for carrying it out. C. d. F.

Salkind, B. Sulla prova proposta da Hollaender per determinare la reazione immunitaria alla tubercolosi. Nota I et II. [**On Hollaender's proposed test for the determination of the immunity reaction against tuberculosis. Notes I and II.**] *Boll. d. Soc. med.-chir. di Pavia*, 1921, **34**, 9, 38.

For carrying out Hollaender's test (*Ztschr. f. Tuberk.*, 1920, **32**, 257) 3 or 4 c.cm. of blood are obtained in a sterile manner from a vein of the arm and poured into a centrifuge tube to be kept for one hour at 37° C. The blood is then centrifuged and the serum, thus separated, transferred into a small test-tube similar to those in use for Widal's reaction. One adds 0·5 c.cm. of physiological salt solution containing 10 per cent. of old carbolized Koch's tuberculin, taking care that the two fluids shall not mix. The test-tube is finally put back into the incubator at 37° C. for twenty-four hours, at the end of which time in some cases nothing special is noticed, while in others a slight cloudiness may be seen at the boundary between one and the other fluid; in yet other cases a distinct ring or a floccular cloudiness are observed. According to Hollaender, in healthy people a negative reaction indicates the absence of a supposed protective substance and consequently their predisposition to tuberculosis. The presence or absence of the reaction in tuberculous subjects would show that the organism is in the condition of opposing or not a valid resistance to the infection. According to Salkind, Hollaender's test is not specific, a zonal reaction being also obtainable with a carbolized physiological salt solution containing no tuberculin, as well as by the use of pure distilled water and very diluted acetic acid. In his opinion the cloudiness between the two fluids is due to the globulins and pseudoglobulins of the serum, and the absence or presence of the reaction, connected with the fact that the amount of globulins and pseudoglobulins contained in the serum varies from one to the other subject, and occasionally even in the same subject. In fact a positive Hollaender reaction can be always obtained with horse serum, which contains a percentage of globulin higher than that of human serum. Similar results were recently obtained by Neumann (*Ztschr. f. Tuberk.*, 1921, **33**, 339). In spite of all this, Salkind comes to the conclusion that 'one cannot exclude the possibility that Hollaender's test may acquire a practical value in cases of tuberculosis and be used to indicate the relation intervening between organism and infection'. C. d. F.

Selter, H. Ueber die Wirkung abgetöteter Tuberkelbacillen. [**On the action of dead tubercle bacilli.**] *Ztschr. f. Hyg. u. Infektionskrankh.*, 1922, **95**, 233.

The author has studied the immunizing properties of killed tubercle bacilli in guinea-pigs. Various preparations of bacilli were employed, but particularly (1) T. B. treated with lactic acid; (2) T. B. killed by carbolic acid; (3) T. B. killed with chloroform and subsequently exposed to the action of pepsin; and (4) T. B. killed with chloroform and subsequently treated with trypsin. Series of guinea-pigs were inoculated with such bacillary products and after twenty-eight days they were subjected to

a subcutaneously administered dose of 500,000 living virulent T. B. None exhibited the slightest trace of immunity as the result of their previous inoculation. In other experiments he found that no tuberculin hypersensitivity was brought about by previous injections of killed cultures of tubercle bacilli. W. B.

Fontana, A. Sull' auto- ed eteroinoculazione del virus dell' Herpes febrilis all' uomo; suo trasporto dalla cornea del coniglio alla cute umana e viceversa. [**Homo- and hetero-inoculation of virus of herpes febrilis in man; its transmission from the cornea of the rabbit to the human skin and *vice versa*.**] *Pathologica*, 1922, **14**, 15.

Continuation of investigations to which reference has already been made (*Medical Science*, 1921–2, **5**, 436). Lipschütz has quite recently shown that the virus of *Herpes genitalis* is transmissible from man to man (*Derm. Wchnschr.*, 1921, **136**, 428). The same results were obtained with the virus of *Herpes labialis* by Fontana, who made successful experiments on himself and various patients. He found, in addition, that, with the contents of corneal vesicles from successfully inoculated rabbits, typical herpetic vesicles can be re-obtained in man. C. d. F.

Wulff, O. Om Vaccinebehandling af Urinvejsinfektioner. [**Concerning vaccine treatment of infections of the urinary tract.**] *Hosp.-Tid.*, 1922, **65**, 17–28, 157–70.

Wulff's paper deals with 108 cases of infection of the urinary tract (gonorrhoea not included) treated at Rovsing's surgical hospital in the period 1911–20. Only 20 were males, and 8 patients were under the age of 15. In 92 cases the germs belonged to the coliform group, in 8 there was a pure staphylococcal infection, in 7 a mixed infection, the urine containing Gram-positive cocci and Gram-negative rods, and in 1 case (renal calculus in a child) streptococci were found. After discarding 8 cases, in which vaccine treatment was prematurely discontinued for various reasons, Wulff tabulates his results thus:

	Albumin.	Pus.	Bacteria.
Before treatment	70%	100%	100%
After treatment	24%	40%	81%

The cases are classified according as they were characterized by acute febrile relapses or by a comparatively insidious course, and some minor groups were reserved for a few cases with rare manifestations. In the first class there were 43 cases, in 21 of which a cure, and in 16 of which improvement, was effected. The most prominent result in this class was the cessation of the acute febrile relapses; various other signs of improvement, difficult to indicate by statistics, were also common. Among the 32 cases (cysto-pyelo-nephritis) in the second class there were 16 terminating in recovery, 10 were improved, and only 6 were unaffected by treatment. A third group contained 17 cases of *pyelitis calculosa*, in 8 of which it was impossible to remove the calculi; hence the failure of vaccine treatment in these cases. In the remaining 9 cases removal of the calculi plus vaccine treatment was followed by a cure in 1 case and improvement in 7. A fourth group included 8 complicated and atypical cases. Omitting these 8 cases and the 8 cases in group 3, in which calculi were retained, Wulff is left with a total of 84 cases which he classifies thus:

	Cured.	Improved.	Unchanged.
Class 1.	21	16	6
„ 2.	16	10	6
„ 3.	1	7	1
Total	38 (45%)	33 (39%)	13 (16%)

In his survey of this subject Wulff recants his quondam belief that infections of the urinary tract run a capricious course which frequently terminates in complete spontaneous recovery. Such spontaneous recovery is in reality exceedingly rare; practically every infection of the urinary tract is chronic. He considers the value of vaccine treatment (autogenous, not stock, vaccines) to be great, although, to judge by his own and others' experiences (he gives a digest of the recent literature), about 20 per cent. do not respond satisfactorily to this treatment. With regard to dosage, he usually begins with 10 to 30 millions; and occasionally he has reached a dosage of 10,000 millions or more. As to the duration of the immunity conferred by vaccine treatment (freedom from relapses), he notes that Schneider puts it at a year to 18 months. In many of his own cases freedom from relapse was maintained for several years, even up to 12 years. Wulff does not classify his cases so as to show the ratio of successful results according as the disease was due to coliform bacilli, staphylococci, or other germs. C. L.

Lussana, S. Batteriemia da bacillo fusiforme con ascesso cerebrale da fissazione. [**Bacteriaemia from *B. fusiformis* with cerebral fixation abscess.**] *Pathologica*, 1922, **14**, 73.

Description of an interesting case in which complete bacteriological and pathological investigations were possible. From the observations made by other authors in similar cases and by the author in the present one, Lussana has reached the following conclusions: There is a form of bacteriaemia from *B. fusiformis* which does not originate from the primary localization in the tonsils but from secondary pulmonary foci. In consequence of this bacteriaemia, abscesses may form in various tissues or organs in which *B. fusiformis* is found associated with other germs, chiefly spirilla and cocci. *B. fusiformis* when inoculated into animals in symbiosis with pyogenic cocci shows a moderate degree of virulence which gets lost in successive passages from animal to animal. In man the abscesses due to *B. fusiformis* may, in spite of their number and size, form in an insidious way and be accompanied only by a moderate degree of fever. Symptoms may even be further reduced to those connected with the anatomical situation of the abscesses. C. d. F.

Levaditi, C., et **Nicolau, S.** Vaccine pure cérébrale. Virulence pour l'homme. [**A pure vaccine prepared from brain and its virulence for man.**] *Compt. rend. Acad. d. sc.*, 1922, **174**, 249.

The authors record the results obtained by using an emulsion of the brain of rabbits, in which an encephalitis had been produced by the local injection of the virus of vaccinia, instead of the usual calf-lymph for vaccinating infants and adults. They find that after numerous cerebral passages in rabbits the virus preserves its specific properties and behaves exactly like the original calf-lymph, with the added advantage of being quite free from bacterial contamination. It can be preserved equally well in the ice chest and at room temperature. J. R. P.

Olitsky, P. Experimental studies on the etiology of typhus fever. IV. Immunizing and toxic agents found occasionally in filtrates of typhus-infected tissues. *J. Exper. M.*, 1922, **35**, 469.

Reference has already been made (*Medical Science*, 1922, **6**, 417) to the previous investigations of the author. In one of these he showed that the virus of typhus in the tissues of guinea-pigs failed to traverse Berkefeld V and N bougies. In the present communication he reports that although the filtrates are apparently free from the infecting agent they can occasionally induce in guinea-pigs not only the typical lesions of the disease but also immunity to subsequent injections of the active virus. W. B.

Jemma, G. Cultura dei parassiti di Leishman dal sangue periferico e coltivabilità di essi in terreni con sangue umano. [**On cultivation of Leishmania from peripheral blood and their development in media containing human blood.**] *Pathologica*, 1922, **14**, 71.

Conclusions: It is possible to cultivate *Leishmania* from the peripheral blood of a certain number of children affected by leishmaniasis. The fact that successful cultures are not more frequently obtained is probably due to the scarcity of *Leishmania* contained in the peripheral blood. The addition of human blood to media used for cultivating *Leishmania* does not, as a rule, prevent their development. There are, however, in the serum of certain subjects substances which appear to hinder the growth of the parasite. C. d. F.

Sangiorgi, G. Di un flagellato dell' intestino umano. [**On a flagellated protozoon of the human intestine.**] *Pathologica*, 1922, **14**, 69.

Description of a new sub-genus and species of the genus *Bodo* for which the denomination *Pirobodo intestinalis* is proposed. This was isolated from the faeces of soldiers, campaigning in Albania, who were apparently affected with dysentery. C. d. F.

Lanfranchi, A., Sani, L., e **Altara, I.** L'intrapalpebro reazione nella diagnosi dell' echinococcosi dei ruminanti domestici. [**The ophthalmic reaction in the diagnosis of echinococcosis in domestic ruminants.**] *Ann. d'ig.*, 1921, **31**, 624.

The ophthalmic reaction is a method of great value for the diagnosis of echinococcosis in ruminants. C. d. F.

Altara, I. Autoantigeno-, emo- e sieroterapia nelle tripanosomiasi sperimentali. [**Autoantigen-, autohaemo-, and autosero-therapy in experimental trypanosomiasis.**] *Ann. d'ig.*, 1921, **31**, 681.

In contradiction to the results obtained by other authors, autoantigen-, autohaemo-, and autosero-therapy were found to have a curative effect neither in experimental trypanosomiasis nor in various infectious diseases. C. d. F.

Sergent, Ed. et Et., Parrot, L., Donatien, A., et **Béguet, M.** Transmission du clou de Biskra par le phlébotome (*Phlebotomus papatasi*, Scop.). [**Transmission of Oriental sore by *Phlebotomus papatasi*, Scop.**] *Compt. rend. Acad. d. sc.*, 1921, **173**, 1030.

Oriental sore is endemic in Biskra, but unknown in Algiers, 600 km. away. The authors experimented with some flies (*Phlebotomus papatasi*) captured in the Military Hospital at Biskra and sent alive to Algiers, where

some were crushed in normal saline and the resulting product rubbed into a freshly scarified area of the forearm of a healthy volunteer. The skin of the arm healed quickly without leaving any scar, but 3 months later the typical lesion of oriental sore appeared at the point of inoculation, and *Leishmania tropica* were found in the contents of the pustule. The authors conclude that *Phlebotomus papatasi* is a natural carrier of the disease.

J. R. P.

Gamna, C. Sull' arteriosclerosi polmonare. [**On arteriosclerosis of pulmonary arteries.**] *Pathologica*, 1921, **13**, 207.

Arteriosclerotic changes of the pulmonary artery and its branches frequently occur in cases of valvular defects of the heart, cardio-vascular malformations and chronic pleuro-pulmonary affections. But such changes should be considered as entirely distinct from the rare, pure, or primary, atherosclerosis of pulmonary arteries. In fact the former changes are, as a rule, limited to the pulmonary artery and to its large and middle-sized branches, while the latter form is characterized by a diffusion of the process over the whole of the pulmonary arteries down to the small and smallest subdivisions and by the absence of any marked lesion of the systemic vessels. This peculiar affection could therefore be termed: *primary pulmonary atherosclerosis*, or briefly *atherosclerotic lung*.

The histological changes of the primary pulmonary atherosclerosis are those typical of atheroma with strongly marked proliferative changes of the intima and media particularly evident along the small and smallest subdivisions and often showing the characteristic picture of *endarteritis obliterans*. Anatomically and clinically the affection is characterized by a progressive dilatation and hypertrophy of the right ventricle of the heart with subsequent insufficiency of the tricuspid valve, leading ultimately to grave circulatory troubles and to the death of the patient. The disease affects particularly young subjects; its pathogenesis is unknown. It appears from an investigation made by the author that the genuine cases published up to the present amount at the most to 23, the oldest one being that of Klob (*Wchnbl. d. Ztschr. d. k. k. Gesellsch. d. Aerzte, Wien*, 1865, **21**, 257). In more recent times, one case was described by Romberg (*Deutsches Archiv f. klin. Med.*, 1891, **48**, 196); one by Aust (*München. med. Wchnschr.*, 1892, **39**, 689); one by Wodynsky (*Jahrb. d. Bosn.-Herzegow. Landesspitals in Serajevo*, Jahrg. 1896, p. 814; referred to by Posselt); two by Mönkenberg (*Deutsche med. Wchnschr.*, 1907, **33**, 1243); one by Kitamura (*Ztschr. f. klin. Med.*, 1908, **65**, 14); one by Rössle (*München. med. Wchnschr.*, 1908, **55**, 377); one by Dürck (*Naturwiss. med. Gesellsch. Jena*; referred to by Gamna); one by Schütte (*Centralbl. f. allg. Path. u. path. Anat.*, 1914, **25**, 483); two by Hart (*Berl. klin. Wchnschr.*, 1916, **53**, 304); two by Krutzsch (*Frankf. Ztschr. f. Path.*, 1920, **13**, 247). To these should be added the observation of Dionisi, mentioned by Gamna as published in 1894, but without any reference; the observations 3rd, 5th, 7th, 9th, and 10th of Rogers (*Quart. J. Med.*, 1909, **2**, 1); the case of Kidd (*Tr. Clin. Soc. London*, 1913, **36**, 219). The case clinically investigated by Borelli (*Atti d. r. Accad. med. di Torino*, 1913 4. s. **19**, 84–90) has now been histologically examined by Gamna together with a recent one, the subject of the present paper. From this series one should strike out the five observations of Rogers because of syphilitic origin; the cases of Romberg and Aust because complicated by congenital malformations of the cardio-vascular system; that of Kidd

because probably belonging to the congenital form of pulmonary atherosclerosis. The genuine cases would thus number only 15. Further details on the subject and allied questions can be found in the recent paper of Krutsch and in the article of Posselt 'Die Erkrankungen der Lungenschlagader' (*Ergebn. d. allg. Path. u. path. Anat.*, 1909, **13**, I. Abt., 298). C. d. F.

Polettini, B. Sulla pretesa trasmissibilità in serie della batteriolisi provocata dal violetto di metile. [**On the supposed transmission in series of bacteriolysis due to methyl violet.**] *Pathologica*, 1922, **14**, 157.

As shown by Botez (*Compt. rend. Soc. de biol.*, 1921, **85**, 385) methyl violet has a bacteriolytic action which can be transmitted in series, but not indefinitely as supposed by Botez. Indeed, the phenomenon is no longer observed when through successive dilutions the quantity of methyl violet has become too small to have a bacteriolytic action. This appears, therefore, due to the disinfecting power of methyl violet and does not essentially differ from that shown by other substances such as corrosive sublimate. There is no relation between the bacteriolytic action of methyl violet and d'Hérelle's phenomenon. C. d. F.

Grosso, G. Sulla reazione di Gaté e Papacostas (*formolgélification*) nei sieri sifilitici. [**On Gaté and Papacostas' formol reaction of syphilitic sera.**] *Pathologica*, 1922, **14**, 46.

Gaté and Papacostas' formol reaction (*Compt. rend. Soc. de biol.*, 1920, **83**, 1432) is not specific and may be positive in various chronic diseases such as carcinomata of the stomach and intestine, tuberculosis, &c. However, it should not be rejected as useless, but reserved as a subsidiary diagnostic method, because it is easily carried out with inactivated or non-inactivated sera and because it is still positive when, after a period of treatment, the Wassermann test has become negative. C. d. F.

Colombo, U. Il siero fresco di topo bianco quale complemento nella prova dell'emolisi. [**On the use of fresh serum of white mouse as haemolytic complement.**] *Gazz. d. osp.*, 1922, **43**, 212.

Fresh serum of white mouse can be used as complement instead of guinea-pig's serum. The quantity necessary to obtain complete haemolysis of red blood corpuscles of ox or sheep is 0·2 to 0·3 c.cm. of the undiluted serum. C. d. F.

Solimano, G. Contributo allo studio delle agglutinine anamnestiche e spontanee. [**Contribution to the study of anamnestic and spontaneous agglutinins.**] *Pathologica*, 1921, **13**, 335.

As long ago as 1909 Dreyer and Ainley Walker (*J. Path. & Bacteriol.*, 1910, **14**, 28) showed that *B. coli* agglutinins, produced in rabbits by inoculations with cultures of *B. coli*, could be stimulated by injections of staphylococci or streptococci or *B. Friedländer*. The term 'anamnestic' is used to indicate the specific agglutinins produced in immunized animals under the influence of heterologous bacteria. The production of anamnestic agglutinins may precede and be greater than that due to the bacteric species used for the secondary inoculation 'as if the organs presumably engaged in the production of agglutinins began, when stimulated to new work, by elaborating first those which they were already accustomed to produce'. The question has been the subject of fresh investigations on the part of

Solimano, who had resort to a strain of *B. dysenteriae*, Shiga, previously used for researches to which reference has already been made (*Medical Science*, 1920–21, **3**, 362). His results do not, in the main, differ from those obtained by Dreyer and Walker and show once more how misleading agglutination tests can be, particularly when used for diagnostic purposes.

C. d. F.

BIOCHEMISTRY

Weir, J. F., Larson, E. E., and **Rowntree, L. G. Studies in diabetes insipidus, water balance, and water intoxication.** *Arch. Int. Med.*, 1922, **29**, 306.

A study of 15 cases of diabetes insipidus. A high incidence of syphilis was noted, but antisyphilitic treatment produced no significant effect. In two instances, in which the onset was sudden, thirst definitely preceded the polyuria. A study of the renal function showed no deviation from the normal except as regards water excretion. Ureteric catheterization showed increased secretion from both kidneys. In all cases pituitary extracts produced a marked effect, which lasted from a few hours up to five days. Attempts at voluntary restriction of fluids proved useless, and caused much suffering to the patients. Metabolism studies showed marked retention of water, and definite retention of chloride under pituitrin treatment, accompanied by an increase in the relative plasma volume and a decrease in the chloride content of the blood. In dogs it was found that pituitary extract definitely checks the production of a water diuresis, and that this effect is still present after section of the renal nerves. Administration of large amounts of water to cases of diabetes insipidus, when under the influence of pituitrin, results in nausea, vomiting, headache, and ataxia. If dogs are given injections of pituitrin subcutaneously and large amounts of water by the stomach tube, symptoms develop when the animal has received approximately 300 c.cm. of water per kilo of body-weight. The first symptoms noted are restlessness, vomiting, and diarrhoea, then drowsiness, muscular twitchings and ataxia, and lastly convulsions and coma which may end in death. The chloride content of the plasma showed a slight decrease, but no increase in the total volume of the blood could be demonstrated by the vital red method. No clinical oedema was noted, and post mortem no free fluid was found in the serous sacs, and the brain appeared to be normal. A rise in the blood-pressure was noted. The symptoms resemble those seen in uraemia.

O. L. V. de W.

Krauss, E. Studien zur Bence-Jones'schen Albuminurie. [**Bence-Jones' albuminuria.**] *Deutsches Arch. f. klin. Med.*, 1921, **137**, 257.

Bence-Jones protein was obtained from the urine from cases of cancer in prisms and fine needles by precipitating with Ehrlich's aldehyde reagent. The site of production of the protein is to be sought for in the cells of the malignant growth itself. The amount appearing in the urine goes hand in hand with the amount of protein metabolism generally, and therefore with the amount of protein taken by the mouth, or may be traceable to any rise

which may be due to a febrile condition. The author thinks that the production of the compound by the cancerous cells is dependent upon the amount of nutritive material brought to them. It might be thought that the body is incapable of dealing with the Bence-Jones protein produced, and for this reason it is excreted in the urine. This is not the case. If it be injected subcutaneously it is catabolized to a certain extent and does not appear as such in the urine. When it was given in this way to a nephritic, the kidney apparently was not able to hold it back to the same extent as in a normal subject. Immunity reactions showed it to behave as a foreign protein. One can get both general and local anaphylaxis in rabbits. Repeated injections of the protein into rabbits produced a nephrosis which is very similar to that encountered in patients suffering from Bence-Jones proteinuria. C. G. L. W.

Schemensky, W. Die Bedeutung der Stalagmone des Urins für die Prognose innerer Krankheiten. [**The stalagmones in the prognosis of internal diseases.**] *Ztschr. f. klin. Med.*, 1921, **93**, 334.

The 'stalagmometric quotient' is defined by the author as the amount of colloidal substances which is excreted by the kidneys into the urine, and this is looked upon as indicating an increase in nitrogenous waste products of high molecular weight. An investigation of nine cases, amongst them acute articular rheumatism, glomerular nephritis, and pulmonary tuberculosis, showed that during the height of the condition the quotient was increased and became lower with recovery. In chronic conditions the quotient was high. In one of two cases where the clinical condition appeared to be better, and the quotient still remained high, there was later a remission. The author believes that the estimation of this quotient is of service for prognostic purposes. C. G. L. W.

Sturgis, C. C., Peabody, F. W., Hall, F. C., and **Fremont Smith, F. The relation of dyspnoea to the maximum minute volume of pulmonary ventilation.** *Arch. Int. Med.*, 1922, **29**, 236.

With the body at rest the demand for oxygen is supplied and the excess CO_2 removed, when 4 to 5 litres of air are breathed per minute. Young subjects, riding a stationary bicycle, attained, when the exercise was most violent, an average minute volume of air of 60·5 litres. This increase in volume is reached by raising the respiration rate to 35 per minute, and by increasing the depth of each respiration until it approximates one-third of the vital capacity of the lungs. A maximum minute volume can be calculated for an individual with sufficient accuracy if one-third of the vital capacity is multiplied by 35. Observations on two individuals during exercise, firstly in a normal condition, and secondly with the vital capacity reduced to one-half by tight chest bandaging, showed that the tendency to dyspnoea varied closely with the percentage of the maximum minute volume that was being used. When the minute volume was 75 per cent. of the calculated maximum definite dyspnoea appeared. O. L. V. de W.

Fraser, F. R., Ross, J. P., and **Dreyer, N. B. The reaction of the blood in relation to dyspnoea.** *Quart. J. Med.*, 1922, **59**, 198.

The dialysation method of Dale and Lovatt Evans was used, and the P_H of both arterial and venous bloods determined. The average reaction of

the blood of healthy young adults by this method is $P_H=7{\cdot}68$, the highest value found being 7·72 and the lowest 7·64. The reactions of arterial and venous bloods are practically identical. Determinations in seven cases of severe heart failure (valvular disease) with orthopnoea indicated that the blood was more alkaline than in health. The degree of alkalaemia did not appear to bear any relationship to the degree of respiratory distress. Severe acidaemia was found in some cases of nephritis, but was not necessarily accompanied by dyspnoea. Reactions of arterial blood as alkaline as $P_H=7{\cdot}95$ and as acid as $P_H=7{\cdot}37$ are compatible with life.

O. L. V. de W.

Macleod, J. J. R., and **Page, S. U.** **The relationship between nervous and hormone control of the respiratory center.** *Am. J. Physiol.*, 1922, **60**, 134.

In decerebrate cats and rabbits the reflex-excitability of the respiratory centre is not altered by changes in the hydrogen-ion concentration and CO_2 tension of the arterial blood. W. C.

Ellinger, P. Zur Pharmakologie der Zellatmung. [**The pharmacology of cell respiration.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 11.

The respiration of erythrocytes (goose) is increased by substances, probably amino-acids, in the endocrine glands. Their action is explained as being due to the fact that they present the cells with extra combustible material. No specific hormones acting on the cell respiration were found in these experiments. Urea causes an increase in the absorbing surface and a consequent increase in the velocity of oxidation. Quinine influences these two factors in the opposite sense. Sodium salicylate is without action on the oxygen usage of erythrocytes. H. W. D.

Campbell, J. A., and **Webster, T. A.** **Effect of severe muscular work on the composition of urine.** *Biochem. J.*, 1922, **16**, 106.

A healthy subject who was accustomed to do 7,500 kgm. of work in five hours developed symptoms of muscular strain on attempting to do 10,000 kgm. in the same time, and showed pathological changes in the composition of his urine. Creatinin, undetermined nitrogen, neutral sulphur, and lactic acid were much increased, whilst acetone bodies were present during part of the experiment. C. G. L. W.

Liljestrand, G., u. **Stenstrom, N.** Versuche über den Gaswechsel und das Minutenvolumen des Herzens bei Massage und passiven Bewegungen. [**Research upon the gas metabolism and the minute volume of the heart in massage and passive movements.**] *Biochem. Ztschr.*, 1922, **127**, 218.

There is an increased consumption of oxygen per litre of blood during massage as compared with a resting period, but no increase of the amount of blood going through the heart (minute volume). R. A. P.

Arnoldi, W. Nachwirkung geringfügiger Einflüsse auf den Stoffwechsel in den nächsten Tagen. [**The after-effects of small procedures on metabolism.**] *Ztschr. f. klin. Med.*, 1921, **92**, 187.

The author shows that evidences of metabolism such as the respiratory exchange and the blood-sugar can be influenced to a marked degree by the previous nutritional history of the patient. He has used for this purpose

an injection of glucose, adrenalin, and salvarsan-silver. The blood-sugar content can be influenced by quite small changes in treatment which have occurred several days previously, and it is remarkable that this delayed influence can be observed for so long a time and is not influenced by the amount of food administered in the interim. C. G. L. W.

Peabody, F. W., and **Sturgis, C. C. The effect of exercise on the metabolism, heart rate, and pulmonary ventilation of normal subjects and patients with heart disease.** *Arch. Int. Med.*, 1922, **29**, 277.

In a group of eleven ambulatory cardiac patients the heart-rate, and the minute volume of the pulmonary ventilation, at rest, were greater than in normals, and the respiration rate was more rapid and shallow. The oxygen consumption at rest averaged 12 per cent. higher, and the pulmonary ventilation 37 per cent. higher than in normals. The response to exercise in cardiac patients is qualitatively the same as in normals, and their greater liability to dyspnoea depends on quantitative limitations.

O. L. V. de W.

Langworthy, C. F., and **Barrett, H. G. Energy-expenditure in sewing.** *Am. J. Physiol.*, 1922, **59**, 376.

Measurements of the energy expenditure of a young woman hemming by hand and sewing on a machine. A respiration calorimeter was used. An interesting observation was made in the course of these experiments on the depressant effect of an attack of influenza on the energy output during rest, when the patient had apparently recovered from the illness. For five weeks after apparent complete recovery with the body-weight returned to normal her energy expenditure was 4 per cent. lower than before her illness.

W. C.

Pincussen, L. Über die Beeinflussung des Stoffwechsels der Kohlenhydrate durch Strahlung. [**The influence of radiation on carbohydrate metabolism.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 127.

On the grounds of certain animal experiments in which it was found that an increased capacity of catabolizing sugar took place under the influence of radiation, the author has attempted to apply the method to diabetics. Various forms of light treatment were used both with and without the preliminary use of eosin as a sensitizer. It was found that in certain cases the blood-sugar content decreased when the patient was given eosin in capsules and thereafter treated for 20 minutes by the radiations from a 'Nitra' lamp placed near the abdomen. This effect is not seen in all cases of diabetes. Those in which there is a large amount of urine excreted show themselves to be refractory. C. G. L. W.

Roth, N., u. **Ernst, Z.** Einfluss der Magenfunktion auf den Kohlenhydratstoffwechsel. [**Influence of the stomach on carbohydrate metabolism.**] *Ztschr. f. klin. Med.*, 1921, **93**, 417.

The respiratory metabolism was estimated by the Zuntz-Geppert apparatus in cases of gastric disturbance and the blood-sugar was estimated at the same time. It was found that the increase in carbohydrate metabolism was delayed when disease of the stomach was present and the blood-sugar curve was flatter than in normal subjects. There was, however, a preliminary

rise in carbohydrate metabolism which the authors put down to stimulation of the pancreas by the high amount of hydrochloric acid present in the stomach, causing a strong diastatic action on the contents of the small intestine. C. G. L. W.

Parnas, J. K., u. **Wagner, R.** Beobachtungen über Zuckerbildung. I. Nach Versuchen, die an einem Falle besonderer Kohlenhydratstoffwechselstörung angestellt wurden. [**Observations upon sugar formation. I. Experiments arising out of a special case of derangement of the carbohydrate metabolism.**] *Biochem. Ztschr.*, 1922, **127**, 55.

Pollak, L. Über den Einfluss von Aminosäuren und Fettsäuren auf die Blutzuckerregulation. [**On the influence of the amino-acids and fatty acids upon the blood-sugar regulation.**] *Ibid.*, 120.

In the paper by Pollak, a new view of the effect of amino-acids, &c., upon carbohydrate metabolism is put forward which will be rather disturbing to some of our conceptions if it is substantiated. Pollak considers that the evidence derived from experiments in which amino-acids fed to phloridzinized dogs have caused the appearance of sugar in the urine does not conclusively establish the view that fresh carbohydrate has been formed from the amino-acids. He thinks that there is a stimulation of the glycolytic function of the liver, produced analogously to an adrenalin effect. If true, this view strikes fundamentally at the conception of the carbohydrate use of de-aminated fatty acid residues from the amino-acids. In support of the new view, rabbits have been injected with amino-acids and with fatty acids. The acids which cause an increase in the blood-sugar are those which are sugar-forming in the diabetic animal. On the other hand, in the case of one experiment upon a starved animal, and in cases where ergotamine was injected together with the substance for experiment, a significant increase was not observed in the blood-sugar. It is held that ergotamine antagonizes the effect of the acid in the same sort of way as it antagonizes the action of adrenalin. It is difficult upon a view of this kind to understand the quantitative relation found by Lusk and his school between the amount of the acid fed and the sugar in the urine. Pollak meets this by saying that there is a quantitative relation between the amount of sugar produced from glycogen and the amount of adrenalin injected into an animal. It is also difficult to see why, upon chemical lines, propionic acid should stimulate glycogen breakdown and not butyric acid.

Besides these indirect criticisms, the paper by Parnas and Wagner records a case which has been abstracted in detail elsewhere (*Medical Science*, 1922, **6**, 161). The case, that of a child of 9 years, is one of a liver tumour. It behaved as if the power of sugar storage was lost. An injection of adrenalin was without effect upon the blood-sugar—in the morning there is no sugar present in the blood. Feeding with proteins, lactates, glycerine, and amino-acids led to a high percentage of sugar in the blood. Feeding with fat was without effect upon the blood-sugar. The difference between the behaviour of this case to adrenalin and to these acids is quite in accordance with the orthodox view of a new formation of sugar, and is not in accordance with Pollak's view. (It must be admitted that, valuable as the evidence of this case is, it is hard to see how the questions can be conclusively proved in the intact animal.) R. A. P.

Frankenthal, K. Über den Einfluss des Durstens auf den Stickstoff- und Chlor-Stoffwechsel. [**The influence of thirst on nitrogen and chlorine metabolism.**] *Ztschr. f. klin. Med.*, 1921, **92**, 208.

Decrease in water intake does not give rise to increase in protein metabolism. There is a decrease in the amount of nitrogen eliminated and some of the waste products are retained in the body. By rapidly repeating the periods of thirst the body becomes accustomed to the proceeding and the nitrogen retention is then not so great. The absorption from the bowel is decreased and assimilation of food is not so good. The amount of sodium chloride excreted is dependent on the diet. With small amounts of sodium chloride, the salt is excreted; with larger amounts, a certain proportion is retained. When larger amounts of water are given there is always a certain amount of sodium chloride which is retained in the body.

C. G. L. W.

Martin, E. G.; *idem* and **Jacoby, L. A.** **The application of the All or Nothing principle of nervous conduction and the interpretation of vasomotor reflexes. Vasoconstriction from warmth stimulation.** *Am. J. Physiol.*, 1922, **59**, 394, 400.

In previous papers Martin has developed the view that the character of vasomotor responses depends on the volume of sensory stimulation and not on the existence of specific nerve-fibres. 'Gentle (or limited) sensory stimulation, not arousing mental alertness, typically induces vasodilatation, while reflex vasoconstriction, not dependent on psychic excitation, requires intense or widespread stimulation.' In the second paper it is shown that even application of warmth, if sufficiently widely distributed, produces a local vasoconstriction. Immersion of the lower part of the human body in water at 42° C. was followed in seven seconds by a drop in temperature of the skin of the small of the back, averaging slightly less than 0·2° C. This was accompanied by sensations of chilliness and 'goose-fleshing'.

The first deals theoretically with the manner in which vasodilator and vasoconstrictor reflexes are produced. Starting from Lucas's 'all or nothing' principle of nervous conduction, it is concluded that the nature of the vasomotor response depends on the number of nervous impulses which arrive within the cerebral nervous system within a given time from a given area of the periphery. The passage of a large volume of nerve impulses along a nerve produces reflex vasoconstriction, a small or moderate volume of impulse streams induces reflex vasodilatation. There is no evidence, at present, of the existence of specific pressor and depressor nerve-fibres in special nerve-trunks. But in view of Ransom's work it must be admitted that within the spinal cord the paths for pressor and depressor excitations are different. It is held that the principle of reciprocal innervation does not apply to vasomotor reflexes. W. C.

Davis, L. E. **The pathway for visceral afferent impulses within the spinal cord.** *Am. J. Physiol.*, 1922, **59**, 381.

Stimulation of the thoracic sympathetic in cats raises the blood-pressure. A similar effect is produced by stimulation of somatic nerves—for instance, the sciatic nerve, provided that the stimulus is sufficiently strong. But these two impulses are conducted along different paths within the spinal cord. The pressor pathway from the somatic nerves has been shown by

Ransom and his co-workers to be situated in the apices of the posterior horns. This last-named pressor reflex is abolished by bilateral destruction of the apex of the posterior horn and of Lissauer's tract. But such a lesion does not abolish the pressor response from stimulation of the sympathetic. In fact no lesion short of complete transverse section of the cord has been found to abolish this sympathetic response. It is concluded, therefore, that the visceral afferent pathway producing vasomotor and respiratory reflex consists of relays of short fibres with synapses in the grey matter of the cord. The reflex arc is not complete within the cord, the impulses must reach the vasomotor centre in the medulla. W. C.

Byrne, J. Further studies of paradoxical pupil dilatation following lesions of the afferent paths. *Am. J. Physiol.*, 1922, **59**, 369.

The paradoxical pupil reaction (greater sensitiveness to adrenalin) which is obtained after section of the cervical sympathetic can also be elicited after section or severe injury to one sciatic nerve or to one brachial plexus. The pupil reaction is elicited in the homolateral eye after 8 days in injury of the brachial plexus, 10–12 days in injury of the sciatic. Moderate injury of the afferent nerve-bundles, and even extensive injury of the tissue around the plexus without apparent injury to visible nerve-bundle, is followed by a typical paradoxical pupil reaction, which is, however, of much shorter duration. These findings emphasize the fact that an intimate functional relationship exists between the pupil dilator mechanism and every portion of the periphery supplied by the spinal sensory nerves. The author states that this relationship has important clinical significance, since in injuries about the shoulder involving the brachial plexus inequality of the pupil is usually interpreted to mean injury of the cervical sympathetic. He holds that such an interpretation should be made after rigid exclusion of lesions of the peripheral nerves. (Note by abstractor: This last part of the argument is not clear because there is no statement either in the paper or in the protocols that the pupils were unequal after lesion of the peripheral nerves. The difference in the size of the pupils appeared only after the instillation of adrenalin, and the pupil on the side of the lesion was then the larger one.) W. C.

Ritchie, A. P. The reaction of resting and active muscle. *J. Physiol.*, 1922, **56**, 53.

Electrometric observations indicate that there is no appreciable change in the hydrogen-ion concentration of frog's muscle during moderate activity. O. L. V. de W.

Gibson, R. B., Martin, F. T., and van Rennselaar Buell, M. A metabolic study of progressive pseudohypertrophic muscular dystrophy and other muscular atrophies. *Arch. Int. Med.*, 1922, **29**, 82.

The characteristic metabolic features of pseudo-hypertrophic muscular dystrophy are: (1) Those associated with the atrophic condition of the muscles—lowered creatinin excretion, creatinuria, recovery in the urine of ingested creatin, and creatinaemia; (2) disturbances of carbohydrate metabolism—hypoglycaemia, and deficient glycogenesis. O. L. V. de W.

Embden, G., u. Lawaczeck, H. Über die Bildung anorganischer Phosphorsäure bei der Kontraktion des Froschmuskels. [**On the formation of inorganic phosphoric acid in the contraction of frog's muscle.**] *Biochem. Ztschr.*, 1922, **127**, 181.

Previous work by the Embden school has established the origin of lactic acid in muscular contraction from a complex of carbohydrate and phosphate (hexose phosphoric acid). At the time of contraction there is a simultaneous appearance of lactic acid and phosphoric acid in the muscle. This paper deals with the interesting question of the time relations of the appearance of the phosphoric acid in the muscle. By the employment of a liquid air technique, it is found that the quicker a muscle is taken after the beginning of contraction (as short intervals as 0·2 sec. were employed in some cases) the more phosphoric acid does the muscle contain. A fresh muscle plunged into liquid air shows a violent contraction (cold stimulation) and a maximal yield of phosphoric acid. After a short stimulation, a muscle does not show the same degree of contraction in liquid air, and also not so much phosphoric acid. The work is held to be evidence for the rapid splitting off of phosphoric acid at the beginning of contraction, and the subsequent rapid combination of it. Stress is laid upon the fact that phosphoric acid, being a much stronger acid than lactic acid, may have the greater effect in muscular contraction. R. A. P.

Geiger, E., u. Loewi, O. Über Änderung des Cholingehaltes der Froschmuskulatur durch elektrische Reizung. [**On the change of the choline content of the frog's muscle produced by electrical stimulation.**] *Biochem. Ztschr.*, 1922, **127**, 174.

The amount of choline in a frog's muscle is increased by violent stimulation. The proof depends upon the effect of extracts of normal and stimulated muscles upon the frog's heart. The extract from the stimulated muscle has a similar effect to that of an extract of acetyl choline. [It seems to be an interesting proof of the presence of toxic substances in the stimulated muscle and may have some bearing upon the question of creatinin metabolism.] R. A. P.

Rosedale, J. L. The amino acids of flesh. The di-amino acid content of rabbit, chicken, ox, horse, sheep, and pig muscle. *Biochem. J.*, 1922, **16**, 27.

Determinations have been made of the di-amino-acids of the protein and fresh muscle of rabbit, chicken, ox, horse, sheep, and pig, by Van Slyke's method. The red meats show a higher lysin content than the white meats. C. G. L. W.

Crile, G. W., Hosmer, H. R., and **Rowland, A. F. The electrical conductivity of animal tissues under normal and pathological conditions.** *Am. J. Physiol.*, 1922, **60**, 59.

Estimations of the electrical conductivity of various tissues were made. The observations refer to rabbits' tissues and human pathological tissues. A very large number of observations were made. Spinal fluid, bile, and blood have the highest conductivity, liver and lung the lowest, the conductivity of the latter two tissues being only one-tenth that of blood. The conductivity varies under different physiological and pathological conditions. The general conclusion is drawn that 'the intracellular changes in exhaustion

and shock which are revealed by the microscope are paralleled by alterations in electric conductivity, and that both the histologic and the electric changes bear a direct relation to the vitality of the organ'. W. C.

Kuré, K., Maëda, M., u. Toyama, K. Chemische Untersuchung über den Zwerchfelltonus. [**The chemistry of diaphragmatic tonus.**] *Ztschr. f. d. ges. exper. Med.*, 1922, **26**, 176.

The sympathetic tonus of the diaphragm stands in close relation to its protein metabolism. When the tonus is raised the creatin content of the muscle is increased. C. G. L. W.

Grafe, E., u. von Redwitz, E. Zur Rolle der Schilddrüse für die Wärmeregulation und den Fieberstoffwechsel. [**The rôle of the thyroid in temperature regulation and in fever metabolism.**] *Ztschr. f. physiol. Chem.*, 1922, **119**, 125.

The authors are of opinion that the rôle of the thyroid in regulating body temperature is not so important as the work of other investigators might suggest. One experiment, performed on a dog from which the thyroid had been removed, showed that the metabolism during an infective fever (*B. suipestifer*) did not differ from that of a normal animal under similar conditions. H. W. D.

Miura, M. Effects of thyroid, thyroxin, and other iodine compounds upon the acetonitrile test. *J. Lab. & Clin. M.*, 1922, **7**, 349.

Miura confirms the statement of Hunt that desiccated thyroid fed to mice protects them against the toxic action of acetonitrile. No protection was given by potassium iodide or di-iodotyrosin. Thyroxin, given in amounts that furnished one-third of the iodine present in the most active thyroid fed, gave in some instances a greater degree of protection. An increased amount of thyroxin led to loss of weight and decreased protection. O. L. V. de W.

Degener, L. M. Studies on the effect of diet on the weight of the hypophysis and thyroid gland of the albino rat, and on the action of their extracts on the isolated small intestine. *Am. J. Physiol.*, 1922, **60**, 107.

Feeding experiments on 200 rats with different diets, namely, (1) oatmeal and milk, (2) vegetables, (3) meat, (4) standard diet plus potassium-iodide, (5) standard diet plus thyroxin. The effects of these diets on body-weight, weight of thyroid and hypophysis, and physiological activity of the extracts from these two glands, were determined. No significant differences were observed.

An interesting new observation is that the action of the two parts of the hypophysis in the isolated intestine is different and antagonistic. The glandular lobe extract causes a contraction, the nervous lobe extract a relaxation. W. C.

Drummond, J. C., and Cannan, R. R. Tethelin—the alleged growth-controlling substance of the anterior lobe of the pituitary gland. *Biochem. J.*, 1922, **16**, 53.

The suggestion has been made that the pituitary body supplied the hormone which regulated the growth of the body, particularly of the skeleton, and Robertson has claimed that the feeding of the fresh anterior

lobe of the ox to white mice leads to a marked retardation of growth beginning in six to ten weeks after birth, followed by a pronounced acceleration during the twentieth to sixtieth week. He isolated a substance to which he gave the name of 'tethelin', and which he regards as the active growth-controlling principle. The authors found that 'tethelin' is a very impure mixture of substances of the lipoid class. They criticize the conclusion of Robertson on the effect of 'tethelin' and of anterior lobe upon growth, and report experiments which failed to point to any influence upon growth produced by oral administration of anterior lobe to the pituitary gland. C. G. L. W.

Morawitz, P., u. Denecke, G. Über Quellungsvorgänge im subcutanen Gewebe. [**On swelling processes in the subcutaneous tissue.**] *Biochem. Ztschr.*, 1922, **127**, 47.

Views as to the causation of oedema fall into two classes. Firstly, there is the view that oedema-formation is due to injury of the blood-vessel walls with increased permeability; secondly, there is the more modern view associated with the name of Fischer, that oedema is the result of purely physico-chemical factors, initiated by changes in the tissue cells themselves. In this paper an attempt has been made to find out how far the tissues themselves are changed in their properties. For this purpose, agar tablets have been placed in the subcutaneous tissues of rabbits for a period of 24 hours after a previous soaking in sterile Ringer. In normal rabbits such tablets lose weight in 24 hours, whereas in animals poisoned with uranium or interfered with by ligature of the ureters the tablets gain weight. In discussing their results, the authors have excluded the reaction of the tissues as well as the purely osmotic factors as the cause of their effects. It is difficult to see how the result can be other than some form of osmotic effect. R. A. P.

RADIOLOGY

Radiodiagnosis

Faber, K. Om Forholdet mellem Brystkassens Form og Ventriklens Form og Leje. [**The relation between the shape of the chest and the shape and position of the stomach.**] *Ugesk. f. Læger.*, 1922, **84**, 479–90.

Faber classifies in four groups the positions of the stomach, as shown by the X-rays, when the patient stands up after having taken a 'contrast' meal: (1) both the lesser and greater curvature are above the umbilicus; (2) the lesser curvature is above, the greater below the umbilicus; (3) the lesser curvature is below the umbilicus, but not more than 2 cm. below it; and (4) the lower curvature is at least 2 cm. below the umbilicus. The following table shows the frequency with which these four positions of the stomach occur among healthy individuals:

	Men.	Nulliparous Women.	Parous Women.
	(70)	(100)	(30)
(1)	35·7 %	11 %	13·3 %
(2)	48·6 %	68 %	43·3 %
(3)	10 %	10 %	20 %
(4)	5·7 %	11 %	23·3 %

Thus, well-defined gastroptosis, as demonstrated by the X-rays, occurs in every twentieth man, every tenth nulliparous woman, and every fourth or fifth parous woman, although they are in other respects normal. To show the frequency with which the four groups occurred among patients with gastric and intestinal symptoms, but without signs of organic disease such as ulcer, cancer, or severe colitis, Faber publishes the following table, which includes the 368 hospital patients suffering from dyspepsia, constipation, and other minor gastro-intestinal evils studied by the X-rays during the past six years:

	Men.	Nulliparous Women.	Parous Women.
	(107)	(187)	(74)
(1)	35·5 %	10·7 %	7.8 %
(2)	53·2 %	49·2 %	26 %
(3)	5.6 %	10.1 %	18.2 %
(4)	5.6 %	30 %	48 %

This table shows that among hospital patients with dyspepsia gastroptosis of the fourth degree is about twice as common as it is among healthy persons. To ascertain the relation, if any, between the shape of the chest and gastroptosis, Faber has devised a new standard, which he calls the 'epigastric index'. A line a is drawn from the umbilicus to the lower end of the sternum where it joins the ensiform cartilage, and where the seventh ribs meet. At the middle of this line, a, a horizontal line, b, is drawn, its length being determined by the distance between one costal arch and the other. The epigastric index (e. i.) $= \frac{b \times 100}{a}$. Example: $b = 9$, $a = 18$, index $= 50$. The e. i. ranged from 30 to 100 in healthy men, and from 15 to 80 in women. The average for 70 healthy men was 59·3, and for 100 healthy nulliparous women it was 45·4. A comparison of the e. i. with the vertical position of the stomach showed that among nulliparous women the e. i. diminished, as a rule, with the descent of the stomach, the average e. i. among nulliparous women with gastroptosis classed in the fourth group being only 33. The same observation was made among men. In other words, a high index is usually associated with a high position of the stomach. But among parous women the relation between the e. i. and the degree of the descent of the stomach was much less regular, and it was evident that the part played by child-bearing in provoking gastroptosis was so great that the part played by the shape of the thorax was comparatively insignificant. The e. i. among 89 parous women in the four groups (positions of the stomach) was 50, 51·9, 53·8, and 43·7. Thus, in the third group the e. i. was actually higher than in the first group, in which the stomach was wholly above the level of the umbilicus. Faber concludes that among men and nulliparous women the shape and position of the stomach are largely determined by the shape and dimensions of the chest. He also finds that, though the long downwardly displaced stomach in the majority of cases acts normally, it is under a handicap and is frequently associated with dyspepsia, atony, and constipation. C. L.

Main, L. R. Some considerations on dental radiography. *J. Orthodentia & Oral Surgery*, 1921, Feb., p. 91. (*J. de radiol. et d'électrol.*, 1922, **6**, 43.)

The author lays stress on the great part that healthy teeth play in the general health of the individual. Often severe troubles are due to bad teeth

and there should always be close collaboration between the doctor and the dentist. Radiography has made a great step towards this collaboration by allowing a precise diagnosis to be made, which is impossible by clinical methods only. Radiological examination should almost always precede treatment of the teeth; it would often cut short long periods of treatment. By means of its information the dentist would avoid these two dangers: looking after teeth beyond aid, and extracting healthy teeth. To be of full value, radiography should be carried out by an expert, since it is delicate work, and the author shows by striking examples that faults in technique can lead to absolutely false impressions. S. E. L-B.

Schell, A. W., and **Spangler, G. S.** **Some considerations on the standardization of dental radiography.** *J. Orthodentia & Oral Surgery*, 1921, March, p. 152. (*J. de radiol. et d'électrol.*, 1922, **6**. 43.)

The authors formulate certain rules by which dental radiographs can always be made under the same conditions and also comparable negatives obtained in different institutions. The following are the conditions: (1) The tube-holder should always be placed in the same position as regards the chair—for instance, on the right—the tube being opposite the patient and the ray horizontal; (2) the sagittal plane of the head should always be vertical; (3) the line of the crowns of the teeth to be examined should be horizontal; (4) it should be parallel to the axis of the tube (except for the dental Coolidge), that is, perpendicular to the normal ray. In all cases these four rules should be carried out without variation (except for the examination of the lower incisors, when the head should be tilted backwards about 45°). The only variable condition for each region will be the position of the normal ray. The following are the best positions: I. *Superior maxilla*: (*a*) molars: angle of 23° below the horizontal, ray centred on the inferior border of the zygoma and the second molar; (*b*) premolars: angle of 33°, ray centred between the two teeth; (*c*) canines: angle of 40°, ray centred on the tooth; (*d*) incisors: ray perpendicular to the line of the nose, centred between the central incisors. II. *Inferior maxilla*: (*a*) molars: angle of 3° above the horizontal, centred on the second molar immediately in front of the insertion of the masseter; (*b*) premolars: angle of 10°, ray centred between the two teeth; (*c*) canines: angle of 15°, ray centred on the tooth; (*d*) incisors: ray horizontal, centred between the two central incisors. S. E. L.-B.

Tranier, G. La radiographie dentaire. [**Dental radiography.**] *Thèse de Montpellier*, 1921. (*J. de radiol. et d'électrol.*, 1922, **6**, 91.)

Radiography of the teeth gives very important information to the stomatologist. If it be a case of an inflammatory lesion or of dental prothesis, X-rays are of great help in establishing a diagnosis or in aiding treatment. Nevertheless, dentists do not consult radiologists often enough. Tranier's work indicates the information that can be derived from X-rays in dentistry. An important chapter is devoted to indications for use. Dental cysts, abscesses, caries, are revealed by X-rays, which show the extent of the lesion. Root débris, fragments of instruments broken by accident in the dental canal, are visible in radiographs. They are often the cause of complications which may perplex the specialist if he does not

establish his diagnosis by means of X-rays. Many of the accidents due to the evolution of the wisdom tooth would be treated more efficaciously if radiography had revealed it early. The evolution of the second dentition in children can be accurately followed by repeated radiographs.

Many plates illustrate the work and show even to the inexperienced all that can be obtained by this method. The technique is studied in detail; extrabuccal method for the lower molars and premolars; intrabuccal method for the inferior incisors and canines and also for the superior maxilla. The author's incidence indicator appears to be very practicable for facilitating the taking of good negatives. This work will repay reading by all stomatologists; good illustrations of the radiological anatomy of the teeth and of their pathological lesions will be found. S. E. L.-B.

Delherm, L., et **Thoyer-Rozat.** Étude radiologique des gros vaisseaux de la base du cœur. [**Radiological study of the great vessels at the base of the heart.**] *Gaz. d. hôp.*, 1921, May. (*J. de radiol. et d'électrol.*, 1922, **6**, 93.)

The authors have made anatomico-radiological researches on the dead body after injecting the vessels at the base of the heart and placing the subject in the positions generally used in examining the heart. (1) *Frontal position.* The shadow of the ascending aorta projects a little to the right of the sternum; the pulmonary artery stands out clearly to the left of the origin of the aorta; the superior vena cava appears a little behind and distinctly to the right of the ascending aorta, projecting well beyond the sternum. (2) *Oblique right anterior position.* At 30° the two aortic shadows are superimposed, giving the 'glove-finger' image. The pulmonary artery tends to disappear behind the aorta; the vena cava projects to the left of the 'glove finger' on the vertebral column. At about 40° the ascending aorta is on the observer's right, the descending on his left; the vena cava increases the size of the shadow of the latter. (3) *Oblique left anterior position.* At 30° the three parts of the aorta are distinct and form a figure-of-eight curve; at 40° the pulmonary artery just projects into this curve beside the ascending aorta: the superior vena cava projects behind the ascending aorta, with which its shadow blends.

Practical deduction. The subject is examined first of all in the frontal position in which the visibility of the normal aorta is much reduced. Examination in the oblique position alone is of importance in measuring the diameter of the aorta. In practice, then, the first examination is in the oblique right anterior position with the right shoulder at 30° to the screen and the diameter of the aorta is measured orthodiagraphically. To see the aorta from a different aspect and as a sort of control, an examination is made in the oblique left anterior position. The advantage of this position is that the aorta is more visible and the vena cava, being behind it, does not obstruct.

The radiological aspect of the great vessels in pathological conditions. The authors then study the modifications which indicate a lesion under the screen. In aortitis, in the frontal position, the aorta projects distinctly beyond the sternum, the vessel is more opaque, the amplitude of the beats may be exaggerated. These signs are confirmed by those found in the oblique positions. When there is an aneurysm one can see on the screen an illustration of the vascular pedicle sometimes attaining the size of the heart and giving the characteristic image of the 'hour-glass heart'; the

tumour is pulsating and the opacity is often greater than that of the vessel itself. The article, clear and well illustrated, is completed by a study of the pulmonary artery and superior vena cava in pathological conditions.

S. E. L.-B.

Radiotherapy

Béclère, H. La radiothérapie des affections du sang. [**The radiotherapy of blood diseases.**] *J. méd. franç.*, 1921, March, p. 99. (*J. de radiol. et d'électrol.*, 1922, **6**, 9.)

After a review of the work on the action of X-rays, the author sets forth the results that one has the right to expect from radiotherapy (after large personal experience) in chronic forms of leukaemia and other diseases. (1) Lymphatic leukaemia—the necessity of an accurate diagnosis, confirmed by a blood examination, in all cases of gland lesions. Irradiation should be directed upon all groups of glands as well as on the spleen. The results are the following: more or less rapid diminution in size of the glands and spleen; amelioration of the general condition and from the blood-picture point of view a return almost to normal; this condition may last 3–5 years. (2) Myeloid leukaemia (132 observations). The spleen is irradiated in sections 10 cm. square; each zone receiving 3 H. units every fortnight. The immediate results are very good; the splenic mass 'melts like snow under the sun' (Béclère); the blood formula tends to become normal, in particular the myelocyte tending to disappear. Unfortunately these results are not lasting, and if one case has survived $8\frac{1}{2}$ years, the average is less, not going beyond $2\frac{1}{2}$ years. (3) Banti's disease—some authors have obtained a diminution in the size of the spleen. (4) Vaquez's disease—good results have been recorded (Luedin, of Bâle); whole skeleton should be systematically irradiated. (5) Lymphadenoma—the action of X-rays is very hopeful. Finally, by irradiating the spleen, some authors abroad have obtained results in cases of persistent haemorrhages. S. E. L.-B.

Lehmann, P. Les doses fortes en radiothérapie. [**Heavy doses in radiotherapy.**] *Bull. off. Soc. franç. d'électrothér.*, 1921, July, p. 182. (*J. de radiol. et d'électrol.*, 1922, **6**, 99.)

The method of moderate repeated doses is a delusive security against radiodermatitis; it prolongs treatment and in course of time can induce the phenomena of radio-intoxication. Insufficient doses can themselves exert an exciting action. Repeated irradiations can make tumours refractory to the rays. The author believes that heavy irradiations at long intervals should be resorted to. The H. measurement is valueless when using penetrating rays, because this unit has not the same biological meaning after penetration. It is necessary to use a ray of constant composition and to take the reaction of the skin as the sole test of value. The dose to apply will be that capable of producing a slight tanning three weeks after irradiation (such a slight erythema should make a possible late radiodermatitis feared). In practice, after being assured that the source gives a constant ray, one should first find out, by means of a pastille, the time necessary to give 5 H. units; with penetrating rays 8–10 H. units can be applied. Successive trials should then be made to find the exact dose furnished by the installation.

The author considers that, if there be a small intensity in the secondary, the rays are more stable and homogeneous. With the Coolidge tube the proportion of soft rays becomes considerably greater for the same length of spark after exceeding 1·5 mm. For an equivalent spark of 20 cm. a filter of 1 cm. of albuminium does not appear to give better results than those from 5 mm. A fresh dose can be applied at the end of a month. When a very sharp reaction is feared (e. g. salpingitis associated with a fibroid) the erythema dose can be made in several applications on consecutive days. It is preferable to use fairly large ports of entry (10 cm. in diameter) since thereby the secondary irradiation in the midst of the tissues is increased. Naturally it is necessary to use all the known contrivances to increase the deep action as compared with the superficial. In practice, if a single application be not enough, the author repeats it after 5 weeks, but believes that in nearly every case, after 3 or 4 irradiations, radiotherapy has done all that it is able to. For three years the author has used this technique with an apparatus of medium power; he has made several thousand irradiations with good results and without accident. S. E. L.-B.

Wertheimer, S. Die Metastasierung bestrahlter und nicht bestrahlter Kollumkarzinome. [**Metastases in irradiated and non-irradiated carcinoma of the neck of the uterus.**] *Strahlentherapie*, 1921, **12**, 90. (*J. de radiol. et d'électrol.*, 1922, **6**, 48.)

It has been stated that metastases are more frequent in irradiated than in non-irradiated cancers. The question is of great importance, since radiotherapy would be valueless if, at the price of local healing, dissemination were brought about in the neighbouring organs. The author publishes the statistics of 104 cases of carcinoma of the neck of the uterus on which post-mortem examinations have been made and sections examined at the Pathological Institute at Frankfort. Of these cases, out of 50 that died without irradiation, metastases were found in 27, i. e. 54 per cent. Of the 54 cases treated with X-rays or radium or the two combined, 26 showed metastases, i. e. 48·15 per cent. Metastases in the liver appeared to the author to be more frequent: 25·9 per cent. in irradiated and 14 per cent. in non-irradiated cases. The same statistics show that the number of cases of metastases diminishes with the age of the patient. S. E. L.-B.

Moulonguet, A. Le traitement du cancer de l'œsophage. [**The treatment of cancer of the oesophagus.**] *Rev. méd. franç.*, 1921, January, p. 300. (*J. de radiol. et d'électrol.*, 1922, **6**, 51.)

When cancer of the oesophagus is diagnosed, gastrostomy is performed before treating the patient with radium. This operation allows (1) the tube to be left in place for several days and the patient to be fed; (2) the oesophagus to be rested. The radium-holder consists of small sealed glass tubes of emanation. Each of these is surrounded by a 1·5 mm. platinum sheath and 0·2 mm. of aluminium. The apparatus is placed in position by using the oesophagoscope. The number of tubes is calculated so that in four days the total irradiation emitted is 15–30 millicuries. Two other methods are also used; the radium puncture of Regaud and the method of unfiltered tubes used in America. S. E. L.-B.

Radium Therapy

Rubens-Duval, H. Radiumthérapie et défense de l'organisme contre le cancer épithélial. [**Radium therapy and the defence of the organism against epithelial cancer.**] *Bull. de l'Inst. Pasteur*, 1921, **19**, 334. (*Arch. d'électric. méd.*, 1921, **29**, 347.)

In the early researches the action of radium was considered to be purely destructive: a selective caustic action which killed the neoplastic cells and left the healthy cells untouched. Dominici and his pupils did not agree with this conception. The rays of radium do not only bring about cytolysis of the neoplastic cells but attack the development of the tumours, hence the irregular growth. The organism itself, according to the author, is able to fight against the cancer, and in this the rôle of the connective tissue is of great importance and must be considered. In the author's experience epitheliomata with abundant connective tissue stroma, especially if young, offer a good prognosis for radium therapy. Cancer is manifested by a breakdown of equilibrium, which the organism tends to re-establish by a connective tissue reaction: on these lines the connective tissue regulates the epithelial activity. On the other hand there are the active defences of the blood and local defences; these are increased when the malignant cells have decreased in vitality, as for example after X-rays or radium. These phenomena are in reality part of the reactions of the organism. The necessity of saving the connective tissue demands the use of good primary filtration and the careful absorption of the secondary rays, and also avoidance of heavy doses. Rubens-Duval recommends a general form of treatment to augment the defence proper of the organism; it may precede the radium and must continue long after. The rapid development of metastases after radium therapy of the primary tumour is perhaps due in part to the inhibition of the defensive reaction of an intoxicated organism by the reabsorption of the cellular débris. S. E. L.-B.

Radiobiology

Chambers, H., Scott, G. M., and **Russ, S. Experiments upon immunity to tumour growth.** *Lancet*, 1922, i, 212–17.

Mice and rats which are ordinarily susceptible to inoculations of a fairly large variety of tumours can be made immune to such transplantations by previously injecting them with tumour which has been sufficiently irradiated by X-rays or by radium; the dose of radiation necessary is called the lethal dose and is that dose which is just sufficient to prevent growth of the tumour-cells when inoculated into a susceptible animal. The immunity conferred in this way upon an animal is lasting and in this respect stands in contrast to the immunity conferred by normal tissues such as spleen, embryonic skin, blood, &c.

The work of Wedd, Morson, and Russ, on Twort mouse carcinoma has been extended here to two tumours of the rat, and the conditions under which the highest degree of immunity is obtained have been studied. It is found, as was anticipated, that it is much easier to influence the growth of a tumour by immunizing the animal before it is given an inoculation of actively growing tumour-cells than it is to do so after the tumour has got a start. Even so, however, the experiments detailed show that it is possible to influence to some degree an actively growing tumour by inoculating the

animal which is bearing it with a quantity of the same tumour which has received a lethal dose of radiation.

When tumour tissue is given a dose of radiation less than the lethal dose, and then inoculated into a susceptible animal, there is often a prolonged period during which growth appears very doubtful; then the tumour will often start to grow, generally with a much reduced rate of growth. Such a phenomenon has a very striking parallel in the behaviour of malignant growths in the human subject during radiation treatment. It was desirable to see whether such tumour-cells which have been slowed up in their rate of growth conferred any immunity in the animal into which they were inoculated. Experiments on these lines showed that no immunity was conferred in this way; so that it is necessary that the full lethal dose of radiation be given if any immunity is to result; on the other hand, it has been shown by Contamin and the authors cited above that excessive irradiation spoils the immunity-conferring power of the tissue.

Attempts were made to extract an active principle from the irradiated tumour tissue, using Locke's fluid, normal saline, or the serum of the animal as the extraction fluid. All these attempts have so far yielded a negative result. The general impression conveyed by them and other experiments is that the active agent causing immunity is produced from tumour-cells during the process of death after irradiation and that any treatment which causes the immediate destruction of the cell prevents the production of this active body. The bearing of these experiments upon the radiation treatment of malignant disease is twofold. The first is that some degree of immunity may result from the adequate irradiation of a malignant tumour in the body, and the second is that the treatment of a patient with irradiated tumour-cells, after the surgical removal of the growth, may help to set up a state of resistance to the disease. This question is considered in the following paper. S. R.

Kellock, T. H., Chambers, H., and **Russ, S. An attempt to procure immunity to malignant disease in man.** *Lancet*, 1922, i, 217.

The authors, since May 1920, have attempted to immunize patients suffering from cancer against their own tumour-cells. After the operation, the tumour material is sent to the laboratory, where the specimen is cut up with scissors and the growth separated as far as possible from the normal tissues. It is then minced into the middle of a shallow dish and spread into a layer of uniform thickness, with the usual aseptic precautions throughout. It is then exposed to X-rays for a period of time sufficient to ensure a lethal dose; for safety this is arranged to be twice the length of time required in the case of the animal tumours which formed the basis of this experimental investigation.

After the X-ray exposure the minced tumour is sucked into an all-glass syringe, fitted with a wide aperture and canula. The irradiated tumour is then injected into two small abdominal incisions made at the time of operation. The incisions, which are made about an inch long, are made down to the deep fascia and a strong pair of sinus forceps thrust along between the subcutaneous tissues and muscles and then opened out. The pockets thus formed are fan-shaped, with the narrow end upwards, so that injected material tends to be retained; they are purposely made large in order to increase the area of contact between the patient's tissues and the injected material. A large-sized drainage tube is put into each of the openings,

reaching nearly to the bottom of the pocket, and stitches are inserted into the skin so that the wound can be easily closed afterwards.

Details of 12 out of 30 cases treated on these lines are given in the paper. The authors themselves state that the number of cases dealt with is as yet too small and the time that has elapsed too short for any definite opinion as to the value of the method in treatment. It may, however, be said that, with efficient technical precautions, the treatment can be carried out without causing tumour formation in, or having any serious effect upon, the patients so far treated. S. R.

Lacassagne, A. Action des rayons du radium sur les muqueuses de l'œsophage et de la trachée chez le lapin. [**The action of the radium rays on the mucosa of the oesophagus and of the trachea of the rabbit.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 26. (*Arch. d'électric. méd.*, 1921, **29**, 345.)

A radioactive capsule can be placed in the lateral cervical region so that it is equidistant from the oesophagus and trachea, and its rays act with like intensity on the epithelium of each. To effect this the author has used tubes of radium in platinum needles. The method of insertion into a rabbit so that the needle is 8–10 mm. from the mucosa is described. A summary of two experiments in which the dose and time of irradiation differed show the difference in radiosensibility of the two mucosae. (1) Two tubes, each containing 26 millicuries of emanation (0·3 mm. and 0·15 mm. platinum needles), were fixed on the right and left sides of a rabbit. The dose given corresponded to the destruction of 5·5 millicuries for each tube. The animal died on the seventh day, after inability to swallow from the third day. The epithelium of the trachea was intact; that of the oesophagus profoundly altered, showing the lesions usually seen in squamous epitheliomata after irradiation. (2) One tube, containing 53 millicuries of emanation in a platinum needle 0·15 mm. thick, was fixed on the right side of the neck of a rabbit and left in place till the animal was killed a fortnight later. The destruction of the emanation was 48 millicuries. The epithelium of the trachea was intact; that of the oesophagus had disappeared entirely. There were also changes in the lumen. *Conclusions.*—The epithelium of the oesophagus of the rabbit is peculiarly sensitive to the rays of radium which, under the same conditions, leave the epithelium of the trachea intact.

S. E. L.-B.

Sonne, C. Action spécifique exercée sur l'organisme par les radiations lumineuses. [**The specific action exerted by light rays on an organism.**] *Compt. rend. Soc. de biol.*, 1921, **84**, 430. (*Arch. d'électric. méd.*, 1921, **29**, 349.)

The author has proved that the rays in question are able to raise the blood of the skin and subcutaneous tissues to a very high temperature—to the highest temperature reached during fever. The results published have been obtained by calculations based on the number of calories absorbed in the irradiation with various rays and by the estimation of the skin temperatures. By means of the thermo-needle the author has directly and simultaneously raised the temperature of the skin and that of the deep tissues during different irradiations, which has led him to state that in light irradiation one establishes, from the surface to within, an elevation of temperature, whereas in heat irradiation a fall occurs. The raising of the temperatures produced in the subcutaneous tissue has given an approximate

value of 44° for luminous rays and 39° for infra-red rays. The author has done some experiments on the influence of various rays on the skin and body of guinea-pigs in which the part of the back exposed to the rays had been shaved. With a white guinea-pig, using light rays, a relatively small degree of heat produced an appreciable rise in the body temperature without burning the skin, whereas with infra-red rays considerable burning is produced without appreciably raising the body temperature. The method of exposing the animal to the rays is described. Five guinea-pigs were exposed and all showed an appreciable increase in body temperature by light irradiation and none or very little by infra-red irradiation.

S. E. L.-B.

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